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L7: Entry 75 of 75 File: USPT Oct 4, 1994

US-PAT-NO: 5352447
DOCUMENT-IDENTIFIER: US 5352447 A

TITLE: Immunotoxins for treatment of intracranial lesions and as adjunct to chemotherapy

DATE-ISSUED: October 4, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Johnson; Virginia	College Park	MD		
Youle; Richard J.	Garrett Park	MD		

US-CL-CURRENT: 424/183.1; 424/832, 514/12, 514/21, 514/8, 530/391.7, 530/394

CLAIMS:

We claim:

1. A method of treating central nervous system tumors or prophylaxing against metastatic lesions to the central nervous system comprising administering a tumor-inhibiting amount of a conjugate comprising a diphtheria toxin, wherein said diphtheria toxin lacks an active cell binding activity, attached to a moiety which binds to transferrin receptors, wherein said moiety which binds to transferrin receptors is selected from the group consisting of an anti-transferrin receptor antibody and transferrin, and wherein the mode of administration is intracranial or intrathecal.

2. A method of treating central nervous system tumors according to claim 1, wherein said mutant diphtheria toxin is selected from the group consisting of CRM102, CRM103 and CRM107.

3. A method of treating central nervous system tumors according to claim 2, wherein said mutant diphtheria toxin is CRM103.

4. A method of treating central nervous system tumors according to claim 2, wherein said mutant diphtheria toxin is CRM107.

5. The method of claim 1, wherein the conjugate is administered intrathecally.

6. The method of claim 1, wherein the conjugate is administered intraventricularly.

7. The method of claim 1, wherein the conjugate is administered into the cavity cavity left by a surgical resection of the tumor.

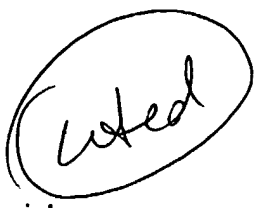
8. The method of claim 1, wherein the central nervous system tumor treated or

the metastatic lesion to the central nervous system prophylaxed against are secondary tumors arising from a primary breast malignancy.

9. The method of claim 1, wherein the central nervous system tumor treated or the metastatic lesion to the central nervous system prophylaxed against are secondary tumors arising from a primary lung malignancy.

10. The method of claim 1, wherein the central nervous system tumor treated or the metastatic lesion to the central nervous system prophylaxed against are secondary tumors arising from a primary prostate malignancy.

DOCUMENT-IDENTIFIER: US 6827931 B1
TITLE: Method for treating endocrine disorders



CLAIMS:

1. A method for treating an endocrine condition, the method comprising the step of intracranial administration of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G to the hypothalamus or pituitary of a patient, thereby treating a symptom of an endocrine condition by reducing a secretion of a hypothalamic or pituitary hormone or releasing hormone, wherein the endocrine condition is selected form the group consisting of gametogenesis, menstruation, acromegaly, gigantism, Cushing's disease, hypergonadism and hyperthyroidism.

2. The method of claim 1, wherein the botulinum toxin is botulinum toxin type A.

3. The method of claim 1, wherein the botulinum toxin is administered in an amount of between 10.sup.-2 units and 500 units.

5. The method of claim 1, wherein the botulinum toxin is administered to the median eminence region of the hypothalamus.

6. The method of claim 1, wherein the botulinum toxin is administered to the anterior pituitary.

7. The method of claim 1 wherein the botulinum toxin is administered to the posterior pituitary.

8. The method of claim 1, wherein the intracranial administration step comprises the step of implantation of a controlled release botulinum toxin system.

9. A method for treating an endocrine condition, the method comprising the step of intracranial administration of a therapeutically effective amount of a botulinum toxin type A to the hypothalamus or pituitary of a patient, thereby alleviating a symptom of an endocrine condition by reducing a secretion of a hypothalamic or pituitary hormone or releasing hormone, wherein the endocrine condition is selected form the group consisting of gametogenesis, menstruation, acromegaly, gigantism, Cushing's disease, hypergonadism and hyperthyroidism.

10. A method for treating an endocrine condition, the method comprising the steps of: (a) selecting a neurotoxin with hypothalamic releasing hormone suppressant activity: (b) choosing a hypothalamic target tissue which influences an endocrine disorder; and (c) intracranially administering to the target tissue a therapeutically effective amount of the neurotoxin selected, thereby treating the endocrine condition by reducing a secretion of a hypothalamic releasing hormone, wherein the neurotoxin is a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G and wherein the endocrine condition is selected form the group consisting of gametogenesis, menstruation, acromegaly, gigantism, Cushing's disease, hypergonadism and hyperthyroidism.

11. A method for treating hypergonadism, the method comprising the step of in vivo local administration of a therapeutically effective amount of a botulinum toxin type A to a cholinergically influenced hypothalamic tissue to a human patient, thereby alleviating a symptom of hypergonadism in the patient by reducing a secretion of hypothalamic hormone or releasing hormone.

12. A contraceptive method comprising the step of intracranial administration to a hypothalamus or

pituitary of a patient of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G, thereby reducing a hypothalamic or pituitary secretion of a hormone or releasing hormone required for gametogenesis.

13. The method of claim 12, wherein the botulinum toxin is botulinum toxin type A.

14. A method for inhibiting ovulation, the method comprising the step of intracranial administration to a hypothalamus or pituitary of a patient of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G, thereby reducing a hypothalamic or pituitary secretion of a hormone or releasing hormone which influences ovulation.

15. The method of claim 14, wherein the botulinum toxin is botulinum toxin type A.

16. A method for inhibiting sperm production, the method comprising the step of intracranial administration to a hypothalamus or pituitary of a patient of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G, thereby reducing a hypothalamic or pituitary secretion of a hormone or releasing which influences sperm production.

17. The method of claim 16, wherein the botulinum toxin is botulinum toxin type A.

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L7: Entry 57 of 75 File: USPT Nov 11, 2003

DOCUMENT-IDENTIFIER: US 6645500 B1
TITLE: Method for down-regulating osteoprotegerin ligand activity

CLAIMS:

8. The method according to claim 7, wherein the epitope is selected from a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a P. falciparum CS epitope.

13. The method according to claim 8, wherein the Tetanus toxoid epitope is P2 or P30.

16. The method according to claim 1, wherein an effective amount of the OPGL polypeptide or the OPGL analogue is administered to the animal via a route selected from the group consisting of the parenteral route; the peritoneal route; the oral route; the buccal route; the sublinqual route; the epidural route; the spinal route; the anal route; and the intracranial route.

Summary of Invention Paragraph:

[0010] Although the cause of schizophrenia is not precisely known, there are several hypotheses regarding the causes. One hypothesis is that schizophrenia is associated with increased dopamine activity within the cortical and limbic areas of the brain. This hypothesis is supported by the therapeutic effects achieved by antipsychotic drugs that block certain dopamine receptors. In addition, amphetamine use may be associated with schizophrenia-like psychotic symptoms; amphetamines act on dopamine receptors.

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L7: Entry 58 of 75 File: USPT Sep 23, 2003

DOCUMENT-IDENTIFIER: US 6623742 B2
TITLE: Methods for treating fibromyalgia

CLAIMS:

1. A method for treating fibromyalgia, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a peripheral location of a body of a patient afflicted with fibromyalgia, wherein the peripheral location is not a locus of pain, and wherein the locus of pain and the site of administration are located within a same dermatome, thereby relieving a fibromyalgia pain for at least one month.

4. The method of claim 1 wherein the peripheral location is in a cranial area or a facial area of the patient, and wherein the locus of pain is at a fibromyalgia tender point.

5. The method of claim 1 wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F, and G.

6. The method of claim 1 wherein the botulinum toxin is a botulinum toxin type A.

8. The method of claim 1 wherein the botulinum toxin is administered with a needle.

9. The method of claim 1 wherein the botulinum toxin is administered by needleless injection.

10. A method for treating fibromyalgia pain, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a peripheral location of a body of a patient, wherein the patient has a locus of pain at a fibromyalgia tender point, and wherein the peripheral location is not at the locus of pain, and the locus of pain and the site of administration are located within a same dermatome, thereby relieving the pain for at least one month.

12. The method of claim 10 wherein the botulinum toxin is selected from the group consisting of botulinum neurotoxin types A, B, C, D, E, F, and G.

13. The method of claim 10 wherein the botulinum toxin is a botulinum toxin type A.

15. The method of claim 10 wherein the botulinum toxin is administered with a needle.

16. The method of claim 10 wherein the botulinum toxin is administered by needleless needleless injection.

17. A method for treating fibromyalgia, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a dermatome of a patient afflicted with fibromyalgia, wherein the dermatome encompasses 50% or more of a locus of pain, wherein the

administration is not at the locus of pain, thereby relieving a fibromyalgia pain for at least one month.

18. The method of claim 17 wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F, and G.

19. The method of claim 17 wherein the botulinum toxin is a botulinum toxin type A.

21. The method of claim 17 wherein the botulinum toxin is administered with a needle.

22. The method of claim 17 wherein the botulinum toxin is administered by needleless needleless injection.

23. A method for treating fibromyalgia pain, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a dermatome of a patient, wherein the patient has a locus of of pain at a fibromyalgia tender point, wherein the dermatome encompasses 50% or more of the locus of pain, and wherein the administration is not at the locus of pain, thereby relieving the pain for at least one month.

26. The method of claim 23 wherein the botulinum toxin is selected from the group consisting of botulinum neurotoxin types A, B, C, D, E, F, and G.

27. The method of claim 23 wherein the botulinum toxin is a botulinum toxin type A.

29. The method of claim 23 wherein the botulinum toxin is administered with a needle.

30. The method of claim 23 wherein the botulinum toxin is administered by needleless needleless injection.

31. A method for treating fibromyalgia, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin type A to a dermatome of a patient afflicted with fibromyalgia, fibromyalgia, wherein the dermatome encompasses 50% or more of a locus of pain which is at a fibromyalgia tender point, and wherein the local administration is not at the locus of pain, thereby relieving a fibromyalgia pain for at least one month.

32. A method for treating fibromyalgia pain, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin type A to a dermatome of a patient, wherein the patient has a locus of pain which is at a fibromyalgia tender point, wherein the dermatome encompasses 50% or more of the locus of pain, and wherein the administration is not at the locus of pain, thereby relieving the pain for at least one month.

DOCUMENT-IDENTIFIER: US 6113915 A
TITLE: Methods for treating pain

CLAIMS:

1. A method for treating pain, the method comprising the step of intraspinal administration of an effective amount of a botulinum toxin to a mammal, thereby alleviating pain experienced by the mammal, wherein the botulinum toxin is not attached to a non-neurotoxin protein.

2. The method of claim 1, wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F and G.

3. The method of claim 2, wherein the botulinum toxin is botulinum toxin type A.

4. The method of claim 1, wherein the botulinum toxin is administered in an amount of between about 10.sup.-3 U/kg and about 60 U/kg.

5. The method of claim 4, wherein the botulinum toxin is administered in an amount of between about 10.sup.-2 U/kg and about 50 U/kg.

6. The method of claim 5, wherein the botulinum toxin is administered in an amount of between about 10.sup.-1 U/kg and about 40 U/kg.

7. The method of claim 6, wherein the botulinum toxin is administered in an amount of between about 1 U/kg and about 30 U/kg.

8. The method of claim 6, wherein the botulinum toxin is administered in an amount of between about 1 U/kg and about 20 U/kg.

12. The method of claim 1, wherein the botulinum toxin is administered intrathecally.

13. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a cranial region of the central nervous system.

14. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a cervical region of the central nervous system.

15. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a thoracic region of the central nervous system.

16. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a lumbar region of the central nervous system.

17. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a sacral region of the central nervous system.

18. The method of claim 1, wherein the administration step includes the steps of:

(a) accessing an intraspinal subarachnoid space of the mammal, and;

(b) injecting the botulinum toxin into the subarachnoid space.

31. A method for the in vivo attenuation of a nociceptive activity of a human patient, the method comprising the step of intraspinal administration to a human patient a therapeutically effective amount of a botulinum toxin, thereby causing an in vivo attenuation of a nociceptive activity.

33. The method of claim 31, wherein the botulinum toxin is selected from the group consisting of botulinum toxins A, B, C, D, E, F and G.

34. The method of claim 33, wherein the botulinum toxin is botulinum toxin type A.

35. A method for treating pain, the method comprising the steps of:

(a) selecting a botulinum toxin with antinociceptive activity;

(b) choosing a portion of the intraspinal region of a patient which influences a nociceptive activity; and

(c) intraspinally administering an effective amount of the botulinum toxin selected.

36. A method for treating pain, the method comprising the step of administering a pharmaceutical preparation to an intraspinal region or to a dorsal root ganglion of a mammal, thereby alleviating pain experienced by the mammal, wherein the pharmaceutical preparation comprises an effective amount of botulinum toxin which is essentially free of any non-neurotoxin protein.

The following definitions apply herein:

"About" means approximately or nearly and in the context of a numerical value or range set forth herein means ±10% of the numerical value or range recited or claimed.

"Local administration" means direct administration of a pharmaceutical at or to the vicinity of a site on or within an animal body, at which site a biological effect of the pharmaceutical is desired. Local administration excludes systemic routes of administration, such as intravenous or oral administration.

"Neurotoxin" means a biologically active molecule with a specific affinity for a neuronal cell surface receptor. Neurotoxin includes Clostridial toxins both as pure toxin and as complexed with one to more non-toxin, toxin associated proteins

"Intracranial" means within the cranium or at or near the dorsal end of the spinal cord and includes the medulla, brain stem, pons, cerebellum and cerebrum.

Methods for treating neuropsychiatric disorders comprise the step of intracranially administering a neurotoxin to a patient. The neurotoxin is administered in a therapeutically effective amount to alleviate at least one symptom of the disorder. The neurotoxin alleviates the symptoms associated with the disorder by reducing secretions of neurotransmitter from the neurons exposed to the neurotoxin.

A suitable neurotoxin may be a neurotoxin made by a bacterium, for example, the neurotoxin may be made from a *Clostridium botulinum*, *Clostridium butyricum*, or *Clostridium beratti*. In certain embodiments of

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File 135:NewsRx Weekly Reports 1995-2005/Jan W3
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Set   Items   Description
S1   6918   'BOTULINUM TOXIN --INTRAPERITONEAL DRUG ADMINIS' OR 'BOTUL-
            INUM TOXIN --PERIOCULAR DRUG ADMINISTRATI' OR 'BOTULINUM TOXI-
            N' OR 'BOTULINUM TOXIN (BOTOX)' OR 'BOTULINUM TOXIN (THERAPEU-
            TIC USE)' OR 'BOTULINUM TOXIN --CLINICAL TRIAL --CT'
S2   4202   E37-E48
S3   309   'BOTULINUM TOXIN A --DRUG ADMINISTRATION --AD' OR 'BOTULIN-
            UM TOXIN A --DRUG ANALYSIS --AN'
S4   58950   R1:R21
S5   62481   S1 OR S2 OR S3 OR S4
S6   1211553   SKULL? OR INTRACRAN? OR CRANIUM? OR CALVARIUM? OR FACE?
S7   2264   S5 AND S6
S8   3   S7 AND NEUROPSYCH?
S9   654   S7/2002:2004
S10   1610   S7 NOT S9
S11   1569   RD (unique items)
S12   50   TARGET - S10
S13   50   TARGET - S11
S14   72   S11 AND (PSYCHIAT? OR MENTAL?)
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 14/9/1   (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)

0012975362   BIOSIS NO.: 200100147201
Botulinum toxin in the treatment of tics
AUTHOR: Kwak Carolyn H; Hanna Philip A; Jankovic Joseph (Reprint)
AUTHOR ADDRESS: Department of Neurology, Parkinson's Disease Center and
  Movement Disorders Clinic, Baylor College of Medicine, 6550 Fannin St,
  No. 1801, Houston, TX, 77030, USA**USA
JOURNAL: Archives of Neurology 57 (8): p1190-1193 August, 2000 2000
MEDIUM: print
ISSN: 0003-9942
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: To evaluate the safety and efficacy of botulinum toxin
  A (BTX) injections in the treatment of tics in patients with Tourette
  syndrome (TS). Background: BTX is an effective treatment for an
  increasing number of conditions characterized by abnormal muscle
  contractions. BTX may improve not only the motor component of tics, but
  also premonitory sensations that precede tics. Methods: Thirty-five
  patients (30 male, 5 female) were treated with BTX in the sites of their
  most problematic tics. Response to BTX was based on a 0 to 4 clinical
  rating scale (0, no improvement, to 4, marked improvement in both
  severity and function). Questionnaires were administered to evaluate
  patients' impressions of overall efficacy and degree of benefit with
  premonitory sensations. Results: Mean duration of tics prior to initial

injection was 15.3 years (range, 1-62 years) and mean duration of follow-up was 21.2 months (range, 1.5-84 months). The mean peak effect response in 35 patients treated in 115 sessions was 2.8 (range, 0-4); the mean duration of benefit was 14.4 weeks (maximum, 45 weeks); and the mean latency to onset of benefit was 3.8 days (maximum, 10 days). Twenty-one (84%) of 25 patients with premonitory sensations derived marked relief of these symptoms (mean benefit, 70.6%). Total mean dose was 502.1 U (range, 15-3550 U); mean number of visits, 3.3 (range, 1-16); and mean dose per visit, 119.9 U (range, 15-273 U). Sites of injections were as follows: cervical or upper thoracic area (17), upper **face** (14), lower **face** (7), vocal cords (4), upper back and/or shoulder (3), scalp (1); forearm (1), leg (1) and rectus abdominis (1). Complications included neck weakness (4), dysphagia (2), ptosis (2), nausea (1), hypophonia (1), fatigue (1), and generalized weakness (1), which were all mild and transient. Conclusions: Botulinum toxin A injections are an effective and well-tolerated treatment of tics. In addition to improving the motor component of tics, BTX also provides relief of premonitory sensations.
DESCRIPTORS:
MAJOR CONCEPTS: Neurology--Human Medicine, Medical Sciences; **Psychiatry** --Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--patient
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: Tourette syndrome--behavioral and **mental** disorders, nervous system disease, treatment; tics--behavioral and **mental** disorders, nervous system disease, treatment
MESH TERMS: Tourette Syndrome (MeSH); Tic Disorders (MeSH)
CHEMICALS & BIOCHEMICALS: **botulinum toxin** --efficacy, evaluation, safety
MISCELLANEOUS TERMS: premonitory sensations
CONCEPT CODES:
21002 Psychiatry - Psychopathology, psychodynamics and therapy
07004 Behavioral biology - Human behavior
10064 Biochemistry studies - Proteins, peptides and amino acids
12512 Pathology - Therapy
20506 Nervous system - Pathology
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
BIOSYSTEMATIC CODES:
86215 Hominidae

14/9/2 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07405398 Genuine Article#: 161TH Number of References: 36
Title: Electrical and magnetic stimulation techniques for the diagnosis of facial nerve palsy and hemifacial spasm
Author(s): Glocker FX (REPRINT) ; Lucking CH
Corporate Source: UNIV FREIBURG,NEUROL KLIN, BREISACHER STR 64/D-79106 FREIBURG//GERMANY/ (REPRINT); UNIV FREIBURG,NEUROZENTRUM, NEUROL KLIN & POLIKLIN/D-79106 FREIBURG//GERMANY/
Journal: KLINISCHE NEUROPHYSIOLOGIE, 1998, V29, N2 (JUN), P59-65
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Geographic Location: GERMANY
Subfile: CC CLIN--Current Contents, Clinical Medicine;
Journal Subject Category: CLINICAL NEUROLOGY; PHYSIOLOGY
Abstract: Electrophysiological tests are mainly performed for prognostic purposes in patients with facial nerve palsies. Most facial nerve lesions are located **intracranially** . Therefore, electrical stylomastoidal stimulation provides normal results until Wallerian

degeneration has occurred. The technique of magnetic stimulation allows non-invasive examination of the entire facial nerve and contributes substantially to the early differential diagnosis of facial palsies. Bell's palsy patients typically show a unilateral local hypoexcitability of the facial nerve to canalicular magnetic stimulation. Normal canalicular excitability and/or subclinical involvement of the contralateral side are not compatible with Bell's palsy. In this case further examinations (e.g. lumbar puncture, magnet resonance imaging) have to be performed. Blink reflex studies also supply pathological results from the beginning of the palsy, however, do not allow location of the lesion. Therefore, blink reflex studies are not helpful in the differential diagnosis of facial nerve palsies. In patients with hemifacial spasm the blink reflex shows a synkinetic response in the **mentalis** muscle indicating lateral spread of impulses to other fibers in the facial nerve. Selective stimulation of facial nerve branches (e.g. zygomatic and mandibular branch) reveal pathognomonic findings in hemifacial spasm by bidirectional transmission of antidromic impulses between the two branches resulting in delayed (ephaptic) responses.

Descriptors--Author Keywords: facial nerve ; neurography ; magnetic stimulation ; blink reflex ; hemifacial spasm ; ephaptic transmission

Identifiers--KeyWord Plus(R): HUMAN-BRAIN; ELECTROPHYSIOLOGICAL PARAMETERS; **BOTULINUM TOXIN**; MOTOR PATHWAYS; BELLS-PALSY; RESPONSES; MUSCLES; MECHANISMS; EXCITATION; REFLEX

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ROSLER KM, 1989, V52, P1149, J NEUROL NEUROSUR PS
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SPRIK C, 1988, V95, P1042, OPHTHALMOLOGY

14/9/6 (Item 4 from file: 73)

DIALOG(R)File 73:EMBASE

11208140 EMBASE No: 2001222927

Tics and Tourette syndrome: A guide to management in childhood

Grattan-Smith P.J.
Dr. P.J. Grattan-Smith, Department of Neurology, Sydney Children's Hospital, Randwick, NSW Australia

Medicine Today (MED. TODAY) (Australia) 2001, 2/6 (52-61)
CODEN: MTNBC ISSN: 1443-430X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

* Tics are common in children and particularly involve facial muscles. * Tics are temporarily suppressible but this produces a build up of tension and an increasing urge to perform the tic. * Tourette syndrome is defined by the presence of multiple motor and one or more vocal tics, which typically wax and wane in severity. * The diagnosis of Tourette syndrome can usually be made on the clinical features alone and there is no need for investigation. * Most children with tics or Tourette syndrome need no treatment, and in most the symptoms subside by late adolescence. * There is a subgroup of children with Tourette syndrome who have associated disorders and who require **psychiatric** management.

BRAND NAME/MANUFACTURER NAME: catapres; serenace; cogentin; periactin; orap ; risperdal; attenta; ritalin

DRUG DESCRIPTORS:
clonidine--adverse drug reaction--ae; clonidine--drug therapy--dt; clonidine--pharmacology--pd; neuroleptic agent--adverse drug reaction--ae; neuroleptic agent--drug therapy--dt; neuroleptic agent--pharmacology--pd; haloperidol--adverse drug reaction--ae; haloperidol--drug therapy--dt; haloperidol--pharmacology--pd; dopamine 2 receptor blocking agent--adverse drug reaction--ae; dopamine 2 receptor blocking agent--drug therapy--dt; dopamine 2 receptor blocking agent--pharmacology--pd; placebo; antidote --drug therapy--dt; antidote--pharmacology--pd; benzatropine mesilate--drug therapy--dt; benzatropine mesilate--pharmacology--pd; cholinergic receptor blocking agent--drug therapy--dt; cholinergic receptor blocking agent --pharmacology--pd; beta adrenergic receptor blocking agent--drug therapy --dt; beta adrenergic receptor blocking agent--pharmacology--pd; cyproheptadine--drug therapy--dt; cyproheptadine--pharmacology--pd; alpha tocopherol--drug therapy--dt; alpha tocopherol--pharmacology--pd; caffeine --drug therapy--dt; caffeine--pharmacology--pd; pimozide--adverse drug reaction--ae; pimozide--drug therapy--dt; risperidone--adverse drug reaction--ae; risperidone--drug therapy--dt; serotonin uptake inhibitor --drug therapy--dt; tetrabenazine--drug therapy--dt; dopamine receptor stimulating agent--drug therapy--dt; benzodiazepine--drug therapy--dt; nicotine--drug therapy--dt; calcium channel blocking agent--drug therapy --dt; naltrexone--drug therapy--dt; lithium--drug therapy--dt; carbamazepine--drug therapy--dt; cannabis--drug therapy--dt; **botulinum toxin** --drug therapy--dt; methylphenidate; dexamphetamine

MEDICAL DESCRIPTORS:
*Gilles de la Tourette syndrome--diagnosis--di; *Gilles de la Tourette syndrome--drug therapy--dt; *Gilles de la Tourette syndrome--etiology--et; *Gilles de la Tourette syndrome--surgery--su; *Gilles de la Tourette syndrome--therapy--th
tic--diagnosis--di; tic--drug therapy--dt; tic--etiology--et; tic--surgery --su; tic--therapy--th; childhood disease--diagnosis--di; childhood disease --drug therapy--dt; childhood disease--etiology--et; childhood disease --surgery--su; childhood disease--therapy--th; **face** muscle; motor dysfunction; speech disorder; disease severity; clinical feature; symptom; disease association; **psychiatric** treatment; child **psychiatry** ; differential diagnosis; chorea minor; heredity; Streptococcus infection; disease course; prognosis; health education; behavior therapy; relaxation training; drowsiness--drug therapy--dt; drowsiness--side effect--si; bradycardia--side effect--si; restlessness--side effect--si; dystonia--drug therapy--dt; dystonia--side effect--si; parkinsonism--drug therapy--dt; parkinsonism--side effect--si; appetite disorder--side effect--si; weight gain; irritability; depression--drug therapy--dt; depression--side effect --si; side effect--side effect--si; akathisia--drug therapy--dt; akathisia --side effect--si; exercise; diet therapy; heart arrhythmia--side effect --si; psychosurgery; drug contraindication; human; male; female; controlled

study; adolescent; child; adult; review
DRUG TERMS (UNCONTROLLED): attenta
CAS REGISTRY NO.: 4205-90-7, 4205-91-8, 57066-25-8 (clonidine); 52-86-8 (haloperidol); 132-17-2 (benzatropine mesilate); 129-03-3, 969-33-5 (cyproheptadine); 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9 (alpha tocopherol); 30388-07-9, 58-08-2 (caffeine); 2062-78-4 (pimozide) ; 106266-06-2 (risperidone); 58-46-8 (tetrabenazine); 12794-10-4 (benzodiazepine); 54-11-5 (nicotine); 16590-41-3, 16676-29-2 (naltrexone); 7439-93-2 (lithium); 298-46-4, 8047-84-5 (carbamazepine); 8001-45-4, 8063-14-7 (cannabis); 113-45-1, 298-59-9 (methylphenidate); 1462-73-3, 51-63-8, 51-64-9 (dexamphetamine)
SECTION HEADINGS:
007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
032 **Psychiatry**
037 Drug Literature Index
038 Adverse Reaction Titles

14/9/17 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

07442795 EMBASE No: 1998359663
Peripherally induced oromandibular dystonia
Sankhla C.; Lai E.C.; Jankovic J.
Prof. J. Jankovic, Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, 6550 Fannin, Houston, TX 77030-3498 United States
Journal of Neurology Neurosurgery and Psychiatry (J. NEUROL. NEUROSURG. PSYCHIATRY) (United Kingdom) 1998, 65/5 (722-728,733)
CODEN: JNNPA ISSN: 0022-3050
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 32

Objectives - Oromandibular dystonia (OMD) is a focal dystonia manifested by involuntary muscle contractions producing repetitive, patterned mouth, jaw, and tongue movements. Dystonia is usually idiopathic (primary), but in some cases it follows peripheral injury. Peripherally induced cervical and limb dystonia is well recognised, and the aim of this study was to characterise peripherally induced OMD. Methods - The following inclusion criteria were used for peripherally induced OMD: (1) the onset of the dystonia was within a few days or months (up to 1 year) after the injury; (2) the trauma was well documented by the patient's history or a review of their medical and dental records; and (3) the onset of dystonia was anatomically related to the site of injury (facial and oral). Results - Twenty seven patients were identified in the database with OMD, temporally and anatomically related to prior injury or surgery. No additional precipitant other than trauma could be detected. None of the patients had any litigation pending. The mean age at onset was 50.11 (SD 14.15) (range 23-74) years and there was a 2:1 female preponderance. Mean latency between the initial trauma and the onset of OMD was 65 days (range 1 day-1 year). Ten (37%) patients had some evidence of predisposing factors such as family history of movement disorders, prior exposure to neuroleptic drugs, and associated dystonia affecting other regions or essential tremor. When compared with 21 patients with primary OMD, there was no difference for age at onset, female preponderance, and phenomenology. The frequency of dystonic writer's cramp, spasmodic dysphonia, bruxism, essential tremor, and family history of movement disorder, however, was lower in the posttraumatic group ($p < 0.05$). In both groups the response to botulinum toxin treatment was superior to medical therapy ($p < 0.005$). Surgical intervention for temporomandibular disorders was more frequent in the post-traumatic group and was associated with worsening of dystonia. Conclusion - The study indicates that oromandibular-facial trauma, including dental procedures, may precipitate the onset of OMD, especially in predisposed people. Prompt recognition and treatment may prevent further

complications.

DRUG DESCRIPTORS:
neuroleptic agent; **botulinum toxin** --drug therapy--dt
MEDICAL DESCRIPTORS:
*jaw disease--drug therapy--dt; *jaw disease--etiology--et; *jaw disease --surgery--su; *jaw disease--therapy--th; *dystonia--drug therapy--dt; * dystonia--etiology--et; *dystonia--surgery--su; *dystonia--therapy--th involuntary movement; muscle contraction; mouth; jaw movement; tongue; idiopathic disease; neck muscle; limb defect; medical record; **face** injury ; surgical injury; disease predisposition; family history; motor dysfunction; onset age; dental surgery; latent period; dysphonia; bruxism; essential tremor; human; male; female; clinical article; aged; adult; article; priority journal
SECTION HEADINGS:
  008 Neurology and Nerosurgery
  011 Otorhinolaryngology
  032 **Psychiatry**
  037 Drug Literature Index

14/9/18 (Item 16 from file: 73)
DIALOG(R)File 73:EMBASE

07243289 EMBASE No: 1998110078
Contemporary ethical dilemmas in psychotherapy: Cosmetic **psychopharmacology and managed care**
Sperry L.; Prosen H.
Dr. L. Sperry, Dept. of Psychiat./Behavioral Med., Medical College of Wisconsin, 9455 Watertown Plank Road, Milwaukee, WI 53226 United States
American Journal of Psychotherapy (AM. J. PSYCHOTHER.) (United States) 1998, 52/1 (54-63)
CODEN: AJPTA ISSN: 0002-9564
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 18

Beyond the traditional ethical dilemmas involving psychotherapy, psychotherapists today are likely to **face** two additional and relatively complex ethical dilemmas: ' **cosmetic** psychopharmacology' and the practice of psychotherapy within managed **mental** health care constraints. Various considerations regarding each of these ethical dilemmas are discussed.

MEDICAL DESCRIPTORS:
*medical ethics; *psychotherapy; *psychopharmacology; *managed care psychotherapist; **mental** health care; human; review
SECTION HEADINGS:
  032 **Psychiatry**
  036 Health Policy, Economics and Management

14/9/28 (Item 26 from file: 73)
DIALOG(R)File 73:EMBASE

05709976 EMBASE No: 1994124219
Aesthetic indications for botulinum toxin injection
Guyuron B.; Huddleston S.W.
29017 Cedar Road,Cleveland, OH 44124 United States
Plastic and Reconstructive Surgery (PLAST. RECONSTR. SURG.) (United States) 1994, 93/5 (913-918)
CODEN: PRSUA ISSN: 0032-1052
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

A clinical trial was undertaken to evaluate the effects of commercially

available botulinum toxin on 14 hyperactive corrugator muscles, 14 procerus muscles, one case of congenital aplasia of the depressor labii inferioris muscle, and one case of iatrogenic injury to the ramus mandibularis branch of the facial nerve with paralysis of the depressor labii and **mentalis** muscles. Of the 31 muscles injected, 28 were appropriately paralyzed with the initial injection. The desired results were obtained in the 3 remaining muscles following a second injection. The ability to frown was nullified in all subjects, resulting in the elimination of glabellar lines. Facial symmetry was achieved in both patients with muscle imbalance. The average duration of the paralysis was 8 weeks, with a range of 2 to 16 weeks. However, this period was prolonged in the latter part of the study with an adjustment of the toxin dose. Our results demonstrate that botulinum toxin injected into overactive facial muscles does produce a predictable and reversible paralysis and eliminates or ameliorates deep frown lines. We also illustrate its use in achieving facial symmetry in one patient with congenitally absent depressor labii inferioris and platysma muscles and in another with postrhytidectomy facial nerve paralysis.

BRAND NAME/MANUFACTURER NAME: **botox** /allergan/United States
MANUFACTURER NAMES: allergan/United States
DRUG DESCRIPTORS:
* **botulinum toxin** --adverse drug reaction--ae; * **botulinum toxin** --clinical trial--ct; * **botulinum toxin** --drug administration--ad; * **botulinum toxin** --drug dose--do; * **botulinum toxin** --pharmaceutics--pr; * **botulinum toxin** --pharmacology--pd
botulinum toxin a
MEDICAL DESCRIPTORS:
*dystonia--therapy--th; *facial nerve paralysis--therapy--th; *facial nerve paralysis--complication--co
adolescent; adult; article; child; clinical article; clinical trial; congenital disorder--therapy--th; ecchymosis--side effect--si; edema--side effect--si; esthetic surgery; **face** muscle; female; headache--side effect --si; human; intramuscular drug administration; male; nausea--side effect --si; paralysis; priority journal; prospective study; rhytidoplasty
CAS REGISTRY NO.: **93384-43-1** (**botulinum toxin a**)
SECTION HEADINGS:
008 Neurology and Nerosurgery
009 Surgery
011 Otorhinolaryngology
037 Drug Literature Index
038 Adverse Reaction Titles

14/9/29 (Item 27 from file: 73)
DIALOG(R)File 73:EMBASE

05576131 EMBASE No: 1993344231
Craniosynostosis as a risk factor
Fehlow P.
Landesfachkrankenhaus Psychiatrie,D-99974 Muhlhausen/Thuringen Germany
Child's Nervous System (CHILD'S NERV. SYST.) (Germany) 1993, 9/6 (325-327)
CODEN: CNSYE ISSN: 0256-7040
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Craniosynostosis is a little known organic factor in sociopathy. This factor should be among those taken into consideration in selecting patients to undergo craniotomy. Among 22 000 **skulls** of neuropsychiatric patients, there were 100 with premature coronal synostosis, compared with 57 with dolichocephaly. Thirty-seven of the 100 patients with coronal synostosis exhibited disorders of social adaptation; frontal cortex functions are assumed to be involved. There were 34 cases of **mental** deficiency, 21 cases of psychosis, 13 of cerebral vascular disease, 10 cases of epilepsy, 4 of acrocephalosyndactyly, 3 of decompensation by slight craniocerebral trauma, and 1 case of ependymoma of the IV ventricle. Dolichocephalic

patients exhibited a stronger tendency towards depressive states and cerebral vascular disease. The risks of **cosmetic** impairment and resulting psychosocial problems are discussed; especially in girls with oxy- and scaphocephaly craniofacial correction, is indicated, as it is also in patients with Saethre-Chotzen syndrome. In cases of premature synostosis of the coronal suture or synostosis of several sutures for carrying out a craniotomy, it is advisable to employ a combination of orbito-fronto-sphenoidal osteotomy for extension of the anterior cranial fossa. Craniosynostosis is a risk factor which, depending on the individual case and the sex and age of the patient, can impair central nervous functions, social adaption, and the blood supply of the brain.

MEDICAL DESCRIPTORS:
*craniofacial synostosis--congenital disorder--cn
article; brain function; craniotomy; frontal lobe; human; major clinical study; personality disorder--complication--co; risk factor; social adaptation
SECTION HEADINGS:
007 Pediatrics and Pediatric Surgery
008 Neurology and Nerosurgery
032 **Psychiatry**

14/9/30 (Item 28 from file: 73)
DIALOG(R)File 73:EMBASE

05423606 EMBASE No: 1993191705
The red face : **Seborrheic dermatitis**
Rebora A.; Rongioletti F.
Istituto di Dermatologia Universita, Viale Benedetto XV, 7,16132 Genoa Italy
Clinics in Dermatology (CLIN. DERMATOL.) (United States) 1993, 11/2 (243-252)
CODEN: CLDEE ISSN: 0738-081X
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH
BRAND NAME/MANUFACTURER NAME: sodium omadine; zinc omadine; danex; flagyl; panoxyl; benzac; benzagel; fostex bpo; selsun blue; tigason
DRUG DESCRIPTORS:
*corticosteroid--drug administration--ad; *corticosteroid--drug therapy--dt ; *imidazole derivative--drug therapy--dt; *isotretinoin--drug therapy--dt; *pyrithione--drug therapy--dt; *pyrithione--drug administration--ad benzoyl peroxide--drug therapy--dt; benzoyl peroxide--drug administration --ad; cimetidine--adverse drug reaction--ae; dithranol--drug administration --ad; dithranol--drug therapy--dt; etretinate; ketoconazole--drug administration--ad; ketoconazole--drug therapy--dt; ketoconazole--drug dose --do; lithium salt--drug administration--ad; lithium salt--drug therapy--dt ; methyldopa--adverse drug reaction--ae; metronidazole; nicotine--adverse drug reaction--ae; penicillamine--adverse drug reaction--ae; pyrithione sodium; pyrithione zinc; selenium sulfide--drug therapy--dt; selenium sulfide--drug administration--ad; shampoo; tar--drug therapy--dt; tar--drug administration--ad
MEDICAL DESCRIPTORS:
*seborrheic dermatitis--complication--co; *seborrheic dermatitis--side effect--si; *seborrheic dermatitis--etiology--et; *seborrheic dermatitis --epidemiology--ep; *seborrheic dermatitis--drug therapy--dt; *seborrheic dermatitis--diagnosis--di
acquired immune deficiency syndrome; candida albicans; climate; differential diagnosis; endocrine function; erythema--etiology--et; **face** disorder--etiology--et; histopathology; human; human immunodeficiency virus infection; immune system; malignant neoplastic disease; **mental** patient; metabolism; neuropsychiatry; nutrition; pityrosporum ovale; pruritus --etiology--et; review; seasonal variation
CAS REGISTRY NO.: 4759-48-2 (isotretinoin); 1121-30-8, 1121-31-9 (pyrithione); 94-36-0 (benzoyl peroxide); 51481-61-9, 70059-30-2 (cimetidine); 1143-38-0, 480-22-8 (dithranol); 54350-48-0 (etretinate);

65277-42-1 (ketoconazole); 555-29-3, 555-30-6 (methyldopa); 39322-38-8, 443-48-1 (metronidazole); 54-11-5 (nicotine); 2219-30-9, 52-67-5 (penicillamine); 15922-78-8 (pyrithione sodium); 13463-41-7 (pyrithione zinc); 56093-45-9, 7446-34-6, 7488-56-4, 8012-80-4 (selenium sulfide); 69912-81-8 (tar)
SECTION HEADINGS:
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reaction Titles

14/9/40 (Item 38 from file: 73)
DIALOG(R)File 73:EMBASE

04327959 EMBASE No: 1990216022
Long-term treatment of involuntary facial spasms using botulinum toxin
Ruusuvaara P.; Setala K.
University Eye Hospital, Haartmaninkatu 4 C,SF-00290 Helsinki Finland
Acta Ophthalmologica (ACTA OPHTHALMOL.) (Denmark) 1990, 68/3 (331-338)
CODEN: ACOPA ISSN: 0001-639X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Botulinum toxin, a powerful pre-synaptic neurotoxin produced by Clostridium botulinum, interferes with the release of acetylcholine from nerve terminals. Since September 1985, we have been using this toxin to treat altogether 62 patients with benign facial spasms. Most of the patients had been on drugs or psychotherapy, 2 had received alcohol injections, 2 had undergone surgery of the orbicular branch, and 2 electrocoagulation of the facial nerve. In essential blepharospasm the duration of the beneficial effect after each treatment with botulinum toxin was about 31/2 months. In patients with hemifacial spasm the response was clearly longer, nearly 5 months in most cases. The treatment gave the best and longest-lasting relief of symptoms in patients suffering from disturbing myokymia. Response was poorest in patients suffering from facial spasms who simultaneously had a severe **psychiatric** disease. The most frequent side effect was mild or moderate ptosis (22.6%). Some patients complained of dry eyes and a few cases displayed facial nerve paresis. Side effects caused by botulinum toxin injections are transient but so also, unfortunately, is the beneficial effect on facial spasms.

DRUG DESCRIPTORS:
* **botulinum toxin**
MEDICAL DESCRIPTORS:
*blepharospasm--drug therapy--dt; * **face** muscle; *hemifacial spasm--drug therapy--dt; *myokymia--drug therapy--dt; *ptosis
major clinical study; human; methodology; male; female; article; priority journal
SECTION HEADINGS:
011 Otorhinolaryngology
012 Ophthalmology
037 Drug Literature Index

14/9/41 (Item 39 from file: 73)
DIALOG(R)File 73:EMBASE

04169166 EMBASE No: 1990051708
Treatment of dystonias and facial dyskinesias
BEHANDLUNG VON DYSTONIEN UND FAZIALEN DYSKINESIEN
Claus D.
Neurologische Klinik mit Poliklinik, Universitat Erlangen-Nurnberg, Schwabachanlage 6, D-8520 Erlangen Germany

Nervenheilkunde (NERVENHEILKUNDE) (Germany) 1989, 8/6 (288-292)
CODEN: NERVD ISSN: 0722-1541
DOCUMENT TYPE: Journal; Review
LANGUAGE: GERMAN
DRUG DESCRIPTORS:
* **botulinum toxin** --drug therapy--dt; *clonazepam--drug therapy--dt; *deanol--drug therapy--dt; *lithium--drug therapy--dt; *physostigmine--drug therapy--dt; *tetrabenazine--drug therapy--dt; *tiapride--drug therapy--dt; *trihexyphenidyl--drug therapy--dt
MEDICAL DESCRIPTORS:
*dystonia--therapy--th; *dystonia--drug therapy--dt
human; review
MEDICAL TERMS (UNCONTROLLED): **face** dyskinesia--therapy--th; **face** dyskinesia--drug therapy--dt
CAS REGISTRY NO.: 1622-61-3 (clonazepam); 108-01-0, 2498-25-1 (deanol); 7439-93-2 (lithium); 57-47-6, 64-47-1 (physostigmine); 58-46-8 (tetrabenazine); 51012-32-9 (tiapride); 144-11-6, 52-49-3 (trihexyphenidyl)
SECTION HEADINGS:
008 Neurology and Nerosurgery
032 **Psychiatry**
037 Drug Literature Index

14/9/68 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01953358 SUPPLIER NUMBER: 66882965 (THIS IS THE FULL TEXT)
Botulinum toxin in otolaryngology: A review of its actions and opportunities for use.
Neuenschwander, Michael C.; Pribitkin, Edmund A.; Sataloff, Robert T.
Ear, Nose and Throat Journal, 79, 10, 788
Oct,
2000
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0145-5613
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 7431 LINE COUNT: 00619

TEXT:
Abstract

Botulinum toxin has several important properties that make it an ideal chemical denervator. These include its high degree of specificity for the neuromuscular junction, its ability to induce temporary and reversible denervation, and its limited degree of side effects and complications. Botulinum toxin is being used safely in a wide variety of clinical settings by many different specialists. In otolaryngologic practice, it is being administered for the treatment of at least a dozen conditions, including various dysphonias, dystonias, and spasms as well as torticollis, facial nerve paralysis, and hyperkinetic facial lines. Studies have shown that botulinum toxin injections have a high rate of success in temporarily relieving symptoms.

Introduction

Botulinum toxin is of interest to otolaryngologists for several reasons. First, it is becoming increasingly popular as a treatment for several otolaryngologic disorders, including spasmodic dysphonias, hemifacial spasms, facial wrinkles, and cricopharyngeal spasms. Second, although its neurotoxic properties have been known for about 100 years, it is only in the past 15 years or so that we have begun to understand its structure and mechanism of action.

Still, there is much we do not know about this substance, and we are in the infancy phase of its use as a diagnostic and therapeutic agent. Ongoing research is helping to clarify some of the less well understood biochemical aspects of botulinum toxin, as well as addressing the problems we **face** in using it as a chemical denervator. Areas of investigation include long-term effects, optimal treatment regimens, and reasons for treatment failure. In this article, we review the development of this

interesting biologic agent in order to clarify its current importance in otolaryngology and its potential for future clinical uses.

History and epidemiology

Botulism is caused by the consumption of contaminated foods, and it can lead to muscle paralysis, suffocation, and death. The disease was first described in the late 1700s, but the toxin itself was not purified until the 1940s. (1) Interest in botulinum toxin was high during World War II, when reports were circulated that Axis countries had developed the capability to use certain toxins against humans. This spurred the United States Army to study botulinum toxin and other biologic toxins. Research continued until 1972, when the United States and several other nations signed the Biological and Toxin Weapons Convention agreement, which called for the termination of research on biologic agents that could be used in warfare. The study of botulinum toxin for therapeutic purposes was carried on by Schantz at the University of Wisconsin and by Scott at the Smith-Kettlewell Eye Research Institute in San Francisco. (1)

In the United States alone, more than 100,000 persons experience some form of involuntary muscle spasm. (1) Botulinum toxin has been used successfully for more than 25 years to treat the pain, disfigurement, and embarrassment that result from dystonias. In 1978, Scott received approval from the U.S. Food and Drug Administration to use botulinum toxin to treat patients with strabismus. In 1989, the FDA approved the substance for use in patients with blepharospasm and hemifacial spasm. To date, these are the only FDA-approved indications. (2)

Structure

Botulinum toxin is a neurotoxin produced primarily by Clostridium botulinum, an anaerobic bacterium. There are seven immunologic types of botulinum toxin--types A through 0. Type A is the most useful clinically, but types B, E, and F are being studied as potential alternatives. (3-5) The gene that encodes the toxin has been isolated and sequenced. (4) The toxin is synthesized as a weakly active, single-chain polypeptide. When it is exposed to a protease, it becomes fully active in the form of a dichain molecule. The dichain is made up of a heavy chain that is responsible for binding to the end-terminal at the neuro-muscular junction and a light chain that is responsible for blocking transmitter release.

Purified toxin is unstable and loses biologic activity overtime. (3) Therefore, hemagglutinin must be added to form the mixture that is intended for human therapeutic use.

Sites of action

Botulinum toxin binds with high affinity to cholinergic nerve endings, including the motor and autonomic nerves. Motor nerves are the most sensitive to the toxin. Small quantities of botulinum toxin can undergo retrograde axonal transport to the central nervous system, but there is no evidence that this has any effect on humans. (4) To exert its effect when injected into muscle, the toxin relies on cell surface receptors to become internalized. In the laboratory, however, botulinum toxin can be injected directly into cells, including non-neural cells, to block acetylcholine release.

Because different serotypes of botulinum toxin do not share the same receptor, they can have slightly different actions inside cells. These differences can be advantageous for clinical medicine. The possibility exists that some patients will respond better to one serotype than another, and a combination of serotypes (chimeras) might be more efficacious than any single one. A combination of serotypes might also permit us to use smaller doses and thus lessen the likelihood of antibody production. (4)

Mechanism of action

Botulinum toxin blocks the release of acetylcholine from cholinergic nerve endings. Three steps are involved in this neuromuscular blockade. First, binding is mediated by the toxin's heavy chain. The receptors are unique and localized to the neuromuscular junction. By itself, this step does not result in transmission blockade. The toxin is internalized by receptor-mediated endocytosis where it resides in an endosome. In the second step, the toxin is released into the cytosol. In step three, the light chain enzymatically blocks exocytosis and the release of acetylcholine at the neuromuscular junction. The toxin does not morphologically change the nerve ending, and it does not cause cell death. (4)

Recovery of function

Botulinum toxin's blockade of transmission is reversible. Recovery from the neurotoxin's effects is partly mediated by the cell body's ability to synthesize and transport material to the nerve ending. (4) Two well-documented effects of paralysis are the sprouting of new nerve terminals and an increase in the number of postjunctional receptors. Experimental evidence in soleus and gastrocnemius muscles indicates that nerve sprouts begin to appear approximately 10 days after neuromuscular blockade and that most nerve terminals demonstrate sprouting after 3 weeks. (6,7) At first, the sprouting is not functional, although some sprouts do make contact over an area outside the neuromuscular junction and do become functional. Abnormalities in the pattern of reinnervation are not uniform and can be prolonged. Evidence also indicates that there is an increase in the number of postjunctional receptors. (4,8) Muscle atrophy occurs during the initial period of denervation, stabilizes, and then dissipates over several mont hs, although microscopic abnormalities might still be seen. (7) Studies confirming the long-term microscopic changes in muscles injected with botulinum toxin are lacking in humans.

There are other reasons for the variability in treatment responses. Muscle fibers can be affected differently by the same dose of toxin. Experimental evidence suggests that fast-twitch muscle fibers remained functionally denervated longer than slow-twitch fibers. (7) This is in contrast to other evidence that suggests that fast-twitch fibers in the thyroarytenoid and lateral cricoarytenoid muscles are reinnervated more rapidly and to a greater degree than slow-twitch fibers. (9) The thyroarytenoid and lateral cricoarytenoid muscles have a high proportion of fast-twitch fibers that are involved in glottic sphincteric action and a low proportion of slow-twitch fibers that are involved in phonation. This might partially explain why the side effects of breathiness and aspiration following botulinum toxin injections are transient while the relief from spasticity is long lasting. Finally, we do not know what effect muscle activity has on the duration of muscle paralysis.

Wong et al demonstrated that responses to b otulinum toxin treatment for spasmodic dysphonia were superior and longer lasting when patients underwent a period of postinjection voice rest. (10) The relationships between botulinum toxin response and muscle type and activity are only now being elucidated.

There are also differences in the duration and degree of response to botulinum toxin that cannot be explained by the aforementioned observations. Some patients who have a good initial response might need larger doses over the duration of treatment. Others experience a reduction in relief from spasm and a shorter duration of response over time. One possible explanation for these diminished responses might be the formation of antibodies to botulinum toxin. However, Biglan et al were unable to identify any antibody response to small doses of botulinum toxin A. (11) Perhaps larger doses--in the range of 300 mouse units (MU) during a 30-day period--might lead to an antibody response. The total cumulative dose might also be a factor in antibody production. Finally, some drugs (e.g., aminoglycoside antibiotics) can potentiate and prolong the effect of botulinum toxin, whereas others (e.g., guanidine and aminopyridines) can limit its effect. (4) The roles of antibody formation and drug potentiation have not been pro ven either clinically or in the laboratory, and they remain incompletely understood.

Types of preparations

There are two commercially available forms of botulinum toxin: Botox and Dysport. Botox is supplied in the United States by Allergan (Irvine, Calif.). A new batch prepared in 1998 contains less albumin than the original batch, which was prepared in 1979. Botox is packaged in vials of 100 MU. Dysport is supplied by Speywood (Wrexham, Wales). It is packaged in vials of 500 MU. The two formulations are not equivalent. Furthermore, either brand's potency can vary among the individual vials in each package, which must be kept in mind when reading the literature and treating patients. The dose required to kill 50% of a batch of mice is 1 MU. The lethal dose for humans has been extrapolated from monkey experiments and is thought to be 2,500 to 3,000 MU, which is well above the common doses used in otolaryngology (usually 1.25 to 75 MU).

The toxin is marketed in a lyophilized form, which must be diluted

with normal saline to obtain the desired concentration. For example, a 100-MU vial that is diluted with 2 ml of saline yields 5 MU/0.1 ml. Different concentrations and different volumes are used for various purposes. For example, because the concentrations are different, a smaller volume can be used for injecting 10 MU into a thyroarytenoid muscle than for injecting 10 MU into the orbicularis oculi.

The FDA recommends that the toxin be used within 4 hours of reconstitution, and it suggests that refreezing leads to a loss of activity. Among the valid concerns about storing toxin for later use are the alteration of its molecular structure, the development of antibodies, inconsistent responses, and irregular dosing patterns. (12) Even so, one study of forearm injections showed that there was no difference in paralysis between patients who had received fresh toxin and those who received toxin that had been refrozen or refrigerated for 2 weeks. (13)

Uses in otolaryngology

Botulinum toxin is being administered for the treatment of at least a dozen conditions in otolaryngologic practice. Among them are two types of spasmodic dysphonia, adductor laryngeal breathing dystonia, blepharospasm, hemifacial spasm, oromandibular dystonia, torticollis, facial nerve paresis with synkinesis, hyperkinetic facial lines, and cricopharyngeal spasm.

Spasmodic dysphonias

Spasmodic dysphonia is probably the most well-known use for botulinum toxin in otolaryngology. Much work in this area has been done by Blitzer and Brin, (14,15) Woodson and colleagues, (16,17) Ford and colleagues, (18,19) and Ludlow and colleagues. (20) Spasmodic dysphonia is believed to be a disorder of central motor processing. It is a focal dystonia, and it is classified as one of two main types. The more common adductor type is characterized by involuntary spasms of the thyroarytenoid and other adductor muscles, which cause a strained or strangled voice. The abductor type is characterized by intermittent hyper-abduction of the vocal folds, which gives the patient a breathy, whispery voice. Although speech therapy might be helpful and should be attempted, most noninvasive therapies are ineffective in controlling symptoms.

A correct diagnosis is essential in the management of patients with laryngeal dystonias. Spasmodic dysphonia must be differentiated from other neurologic disorders that cause voice dysfunction. (17,21) An incorrect diagnosis can result in treatment without effect, worsening symptoms, or even life-threatening complications. Moreover, treatment of a misdiagnosed patient with psychogenic dysphonia might result in a placebo effect that could incorrectly support the inaccurate diagnosis and delay proper treatment.

Adductor spasmodic dysphonia. Injection of botulinum toxin into the thyroarytenoid muscle has been used since 1984 to treat adductor spasmodic dysphonia, and it is considered the treatment of choice. Injections can be administered percutaneously or perorally. Most authorities--including Sataloff, (21) Blitzer and Brin, (15) Woodson, (17) and Adams (22)--use the percutaneous technique. A hollow, Teflon-coated, 27-gauge electromyographic (EMG) needle is used to penetrate the cricothyroid membrane. The needle is then directed superiorly and laterally toward the thyroarytenoid muscle, and the laryngeal lumen is avoided. Confirmation that the proper position has been reached occurs when EMG shows a sharp increase in electrical activity as the patient phonates. The disadvantage of this technique is that it requires an EMG machine and a person who is familiar with the performance and interpretation of laryngeal EMG.

Other authors prefer the peroral technique. (18,23) Because motor endplates are thought to be distributed throughout the muscle, the proponents of peroral injections argue that this technique allows them to more easily diffuse toxin over the entire muscle. (18) Prior to injection, the larynx is anesthetized topically and visualized by indirect laryngoscopy or flexible nasolaryngoscopy. A syringe fitted to a curved laryngeal injection needle is used to deliver botulinum toxin to two sites through the superior surface of the true vocal folds. This technique yields a high rate of success, and patients tolerate it well. Furthermore, Ford suggests that the peroral approach requires smaller doses than the percutaneous technique because localization is more precise, although this ideals controversial. (18,19) The peroral approach also has the advantage of being a technique with which otolaryngologists are already familiar.

Finally, it does not require EMG guidance. Its disadvantages are the need for special needles , the greater amount of time needed to deliver the toxin, the need for an assistant, and the waste of toxin that occurs because some of it remains unused in the catheter. (23)

The size of the dose varies among patients and physicians. Blitzer and Brin first began injecting 2.5 MU unilaterally in patients with adductor spasmodic dysphonia, but they eventually came to believe that this amount had little effect. (15) Once they began injecting an additional 7.5 MU, they noted the onset of vocal fold paresis and prolonged breathiness and a 90% improvement in function. They also attained successful results with bilateral injections of 3.75 MU. Blitzer and Brin have since modified their technique and now start with 1.25 MU bilaterally and titrate the dose upward until optimal function is achieved. They note that complete paralysis is not required to achieve a good outcome. We have reported similar findings. (21)

One of the most useful aspects of botulinum toxin is that it can be titrated to achieve the best possible result in each individual. Doses can range from as low as 1.25 MU to as high as 30 MU, depending on the response, degree of side effects, and technique. Larger doses can lead to greater improvement in vocal function but, of course, they are also associated with a greater degree of side effects. George et al reported that dose-related responses were seen with doses up to 7.5 MU, and complete paralysis was achieved with 10 MU. (24) They concluded that doses smaller than 10 MU are sufficient for clinical paralysis.

In general, patients with adductor spasmodic dysphonia who receive botulinum toxin for the first time should be given a low dose--approximately 1.25 to 2.5 MU bilaterally or 10 to 20 MU unilaterally. They should be followed up within 2 weeks, and the dose should be adjusted as needed. Patients with a paralyzed vocal fold and those who have undergone a nerve section might also benefit from low-dose injections, although their improvement might not be as dramatic. Clinically, results vary among patients, and treatment patterns must be individualized. Results also vary from treatment to treatment in the same patient.

Injections can be administered unilaterally or bilaterally in patients with adductor spasmodic dysphonia, although there is some controversy over the efficacy and degree of side effects with the two techniques. (15,22,25-27) Nevertheless, both techniques result in significant improvements in voice quality and normally cause only minimal and transient side effects. The most common side effects are a short period, usually 1 to 2 weeks, of breathiness or hypophonia, dysphagia, choking, pain at the injection site, and edema of the vocal folds if too much volume is injected. Excessive weakness or more severe side effects can occur if the toxin spreads to other adductor muscles, such as the lateral cricoarytenoid. (24) No significant or long-term side effects have been reported. Microscopic changes in motor units and a prolonged disorganization of motor units have been described, and the process of reinnervation can take as long as 3 years. (20) Longer followup studies are needed to understand the long-term effect s of botulinum toxin.

Bilateral injections are usually administered because weakening or paralyzing only one vocal fold theoretically stresses the other fold and can exaggerate dystonic symptoms. (15) Also, bilateral injections expose the patient to less botulinum toxin because they can be given in a smaller cumulative dose than unilateral injections.

Responses can be minimal or quite dramatic. Studies have shown that success rates are high. (15,16,21,22,28) It has been postulated that by paralyzing the laryngeal muscles and possibly altering a feedback loop, botulinum toxin might modify the inappropriate timing of phonatory muscles in the speech-motor loop, (16,29) but the significance of this action has not been fully studied. Although botulinum toxin therapy might not always result in normal speech, it is a safe and reasonable treatment to restore fluency. Its effect usually becomes evident in 24 to 72 hours; maximum effectiveness is seen in about 2 weeks, and it lasts on average 3 to 6 months, occasionally longer. Some patients have gone into remission. The reasons for this are not clear, but such instances raise questions about the accuracy of the diagnosis.

Abductor spasmodic dysphonia. For patients with abductor spasmodic dysphonia, injections are delivered to the posterior cricoarytenoid muscle,

although cricothyroid injections have also been used. (15,30) These injections usually require EMG guidance. When one is injecting the posterior cricoarytenoid muscle, the larynx is rotated away from the side of the injection and the needle is placed percutaneously into the skin over the lateral aspect of the thyroid ala below its midpoint. EMG confirmation can be achieved by having the patient sniff. The posterior cricoarytenoid muscle can also be reached through the cricothyroid membrane, especially in females and some young men. Peroral injections can also be performed; the cricothyroid is approached through the midline in a lateral and superficial direction. Confirmation of proper needle position is obtained by having the patient sing an ascending scale or slide (glissando) and observing an increase in EMG activity as the pitch increases.

The posterior cricoarytenoid is injected with an initial dose of 3.75 MU, and this amount can be titrated as necessary. (15) If symptoms persist and the posterior cricoarytenoid has already been completely paralyzed, the contralateral posterior cricoarytenoid can be injected cautiously with very small increments of toxin. However, the patient must be willing to accept the risk of airway compromise. In patients who fail this technique, injections into the cricothyroid can be performed. (30,31)

Blitzer et al studied 32 patients with abductor spasmodic dysphonia and found that after subjective pre- and postoperative evaluations by patients, physicians, and speech pathologists, the patients' percentage of normal function improved on average from 31 to 70%. (31) Most of these patients received bilateral posterior cricoarytenoid injections. The authors did not comment on the duration of response. In another study, Ludlow et al treated 10 patients who had abductor spasmodic dysphonia and cricothyroid hyperactivity. (30) They found that six of the 10 patients responded to cricothyroid injections and experienced an increase in sentence duration (the length of time a patient is able to speak without breaks or breaths) and in their proportion of voiced speech. Patients returned for reinjection at 4- to 6-month intervals.

As is the case with patients who have adductor spasmodic dysphonia, results in patients with abductor spasmodic dysphonia vary, but many do obtain benefit from botulinum toxin injections. The most worrisome adverse effects seen with posterior cricoarytenoid injections, especially bilateral injections, are stridor and airway compromise, but they are not common. When stridor does occur, it usually manifests during exertion. Two other fairly common side effects are transient dysphagia and aspiration of fluids.

Special laryngeal applications

Botulinum toxin has been used by one of the authors (R.T.S.) and by others--Andrew Blitzer, MD (oral communication, 1996), Michael Rontal, MD (oral communication, 1997), and Steven Zeitels, MD (oral communication, 1998)--for a variety of special laryngeal problems. The toxin can be used for the treatment of recurrent laryngeal granulomata, as an adjunctive treatment for arytenoid dislocation, and for the management of laryngeal synkinesis associated with reinnervation after recurrent nerve paralysis. We have also considered its use in selected cases of bilateral vocal fold paralysis.

Adductor laryngeal breathing dystonia

The treatment of adductor laryngeal breathing dystonia (respiratory dystonia) with botulinum toxin was described by Grillone et al in 1994, (32) This condition is characterized by a paradoxical adduction of the vocal folds during inspiration, which leads to stridor. The stridor usually disappears during sleep and worsens with exertion. The voice is normal. Many patients experience a respiratory dysrhythmia, and many complain of severe fatigue that can interfere with work. These patients can be treated with botulinum toxin injections into each thyroarytenoid muscle, usually with up to 3.75 MU, depending on the severity of the condition. Treatment can significantly alleviate stridor and fatigue for up to 3 or 4 months. The most common complications are a transient breathy voice and a mild aspiration of liquids.

Blepharospasm

Blepharospasm is a disabling condition that can cause functional blindness. It involves the involuntary activity of the orbicularis oculi, procerus, and corrugator supercilii muscles. Its symptoms include lower facial spasms and oromandibular spasms. Blepharospasm can occur in

isolation or as part of other conditions, such as Meige's syndrome.

Botulinum toxin has been used to successfully treat blepharospasm since 1982, and it is now the treatment of choice. (33-35) The injections can be given with or without EMG guidance. Without EMG guidance, injection sites are determined by palpating the affected muscle groups. A 30-gauge needle is used to inject small doses at several sites laterally, medially, and inferiorly. Patients who do not respond might benefit from brow injections. Injections delivered outside the orbital rim have the shortest duration of action and the least effect, but they also cause the fewest side effects. (36,37) Initial doses range from 2.5 to 5.0 MU per site and are titrated upward to 12.5 to 30 MU per eye. Effects are seen in 2 or 3 days and generally last 3 or 4 months.

Regardless of technique, the central part of the upper eyelid should not be injected in order to avoid paralysis of the levator palpebrae superioris and subsequent ptosis. Diplopia can occur if the toxin enters the extra-ocular muscles. Other side effects include epiphora, ocular irritation, lagophthalmos, and exposure keratitis. On rare occasions, ectropion, entropion, or blurred vision occur. (33,35,36,38) Side effects can occur as a result of the diffusion of toxin, but they can be minimized by injecting smaller volumes and avoiding massage of the region.

Hemifacial spasm

Hemifacial spasm usually begins in the orbicularis oculi, and it can spread to involve the muscles of the brow, lower **face** , and neck. Patients with hemifacial spasm (like those with blepharospasm) might have an underlying neurologic disorder or other condition that is causing their spasm. For example, hemifacial spasm can be caused by a vascular loop compression of the facial nerve, or it might be associated with parkinsonism or another neurologic disorder characterized by involuntary muscle spasms. Regardless of the etiology, botulinum toxin provides temporary relief of symptoms.

Before considering botulinum toxin therapy, it is necessary to conduct a complete evaluation, which can include magnetic resonance imaging, EMG, angiography, neurologic consultation, selected blood tests, and other studies.

Injections can be guided by EMG, but many experienced physicians feel comfortable without it. Patients usually receive 12 to 30 MU distributed in 2.5- to 5.0-MU doses. The toxin is typically injected into the zygomaticus major and minor, the levator anguli oris, and the risorius. Improvement has been reported to occur in 92 to 100% of patients. (35,37-39) The duration of symptom relief extends beyond 4 months on average, but some patients require a reinjection after 10 weeks, sometimes sooner. A few patients have gone into remission. (33) Over time, some patients require larger doses, some can get by with smaller loses, and some are maintained on the same doses. The reasons for this variability are not known.

Side effects include those seen with blepharospasm. substantial facial weakness is noted occasionally. Facial asymmetry, drooling, and chewing problems can also occur. (33,35,36,38) But for many patients, these side effects are inconsequential when compared with the disabling spasms of their disease.

Oromandibular dystonia

Oromandibular dystonia can occur alone or with other focal or generalized dystonias. Spasms of the muscles of mastication can lead to pain, abnormal jaw positioning, temporomandibular joint dysfunction, and trismus. The diagnosis can be difficult. In addition to botulinum toxin, treatments include anticholinergics and benzodiazepines. (40)

Botulinum toxin injections are delivered to those muscles that appear to be the most spasmodic, usually the temporalis, masseter, and medial and lateral pterygoids. Injections into the pterygoids must be made with EMG guidance. Toxin is delivered in one or more injections of 10 MU distributed over the muscle. Doses range from 10 to 40 MU and can be titrated as necessary. (40) The effects of botulinum toxin in oromandibular dystonia are seen in 24 to 72 hours and generally last 10 weeks to 4 months. (40) Patients show significant improvement and are able to return to normal eating and speaking habits without pain.

Torticollis

Botulinum toxin has been used to treat torticollis caused by sternocleidomastoid spasm. Large doses are usually needed, sometimes 100 to

300 MU per sternocleidomastoid muscle. Local complications include dysphagia and neck weakness, and systemic complications include pruritus, nausea, flu-like symptoms, fatigue, generalized weakness, and distant, unrelated muscle weakness. (41,42)

Dysphagia is thought to be caused by toxin diffusion into the constrictor muscles. Toxin diffusion has been shown to be dose-related. The toxin can spread over a large area and even cross fascial planes. Symptom relief lasts 11 weeks on average.(37) The physician should keep in mind concerns over the long-term effects of such large doses, particularly the risk of developing antibodies against botulinum toxin. These doses are also high enough to raise concerns about the development of antibodies to botulinum toxin. (42)

Facial nerve paralysis

The management of patients with facial nerve paresis can be very difficult. Involuntary eyelid closure and other facial movements associated with facial nerve paralysis can be disfiguring. These signs are associated with an aberrant regeneration of the facial nerve. Among the other treatments for facial nerve paralysis are ptosis repair, selective myectomy, and selective neurectomy. But these procedures have their drawbacks, including the weakening of an already denervated muscle, their irreversibility, and the difficulty encountered in achieving optimal results.

Borodic et al studied 12 patients with synkinesis following facial nerve paralysis who received a mean dose of 22 MU of botulinum toxin and found that improvement lasted about 5 months. (43) The authors noted significant improvement in synkinetic movements, but periocular injections increased facial dyssymmetry. Minimizing the dose can limit diffusion.

Patients with facial nerve paralysis often do not regain complete function. Techniques to reanimate the **face** often improve facial symmetry, but they fail to do anything about the pull of the normal contralateral **face** , which can be very deforming. In these patients, botulinum toxin can be injected into the contralateral zygomaticus major and the risorius to improve symmetry at the nasolabial fold and oral commissure. For patients with facial nerve paralysis, the uses of botulinum toxin in rehabilitation, surgical reanimation, and temporary relief of spasm, synkinesis, and asymmetry are evolving. (44)

Hyperkinetic facial lines

Botulinum toxin has been helpful in treating the aging **face** . Glabellar lines, crow's feet, deep forehead lines, and deep nasolabial folds have all been treated successfully. Hyperkinetic lines are a result of pull on the skin by underlying muscles. The procerus and corrugator supercilii create deep lines in the glabella during frowning. Crow's feet are created by the lateral orbicularis oculi during squinting. In the forehead, lines are made by the frontalis muscle. Nasolabial folds are created by the zygomaticus minor, levator labii superioris, orbicularis oris, and levator labii superioris alaeque nasi.

Carruthers et al first noted that patients who were treated for blepharospasm, hemifacial spasm, and Bell's palsy all displayed a loss of wrinkles. (45) Since then, botulinum toxin has been used to lessen or eliminate the degree of hyperfunctional lines of the **face** . (46-49)

EMG can be used to guide the placement of the needle in the treatment of glabellar lines, but once a physician becomes familiar with the technique, EMG can be dispensed with. As is the case in the treatment of other types of muscle spasms, the advantage of using EMG is that if a patient does not respond to the initial injection, specific sites of persistent activity can be identified and subsequent injections can be made with greater precision. If there is an absence of activity, injections can be placed in the orbicularis oculi, corrugator supercilii, and frontalis muscles. It is important to remember that the injections must be placed into the muscles, not the wrinkles. Treatment usually begins with 10 MU into each corrugator supercilli and can be repeated as necessary. (47)

Crow's feet are treated in a similar fashion, usually with EMG guidance. Smaller doses (5 MU) are used to treat each eye. Forehead lines and nasolabial folds are treated with various amounts of botulinum toxin. In each region, treatment can render a graded weakening of the underlying musculature and a partial or complete resolution of the hyperkinetic lines. When treating these areas, small doses are delivered to several sites.

Results can be seen in 5 to 7 days, and the treatment effects last from 2 to 6 months. (48,49) Patients are generally satisfied with their outcomes and return for further therapy. (47) Complications include temporary ptosis, upper lip droop, mild swelling, ecchymosis, and local discomfort.

Botulinum toxin can be an excellent alternative or adjunctive treatment to topical agents, chemical peel, laser resurfacing, soft tissue augmentation, or surgery. No major or long-term complications have been reported following cosmetic botulinum toxin injections. The maximum degree of expected improvement can be simulated by spreading apart the wrinkle to be treated with two fingers. (47) But because improvement is only temporary, some patients opt to discontinue botulinum toxin injection treatment and undergo a permanent but more invasive procedure. However, these approaches are often ineffective and can leave visible incision scars.

Patients who are most likely to fail botulinum toxin injection therapy are those who have thick, sebaceous skin, deep dermal scarring, extraordinarily deep lines, excess skin laxity as a result of aging, incomplete denervation, and accessory muscle function that contributes to the wrinkling. (46,47)

Cricopharyngeal spasm

Botulinum toxin can be used to correct voice failure following tracheoesophageal puncture and dysphagia secondary to cricopharyngeal spasm. Cricopharyngeal spasm has been reported to be a cause of failure of voice restoration following tracheoesophageal puncture in as many as 12% of laryngectomy patients. (50) It is sometimes difficult to make this diagnosis, but a barium swallow, esophageal manometry, and EMG showing persistent spasm on swallow can be helpful. Injection of botulinum toxin into the cricopharyngeus can be used diagnostically and therapeutically in patients who have voice failure or dysphagia secondary to cricopharyngeal hyperactivity, (50,51) Under EMG guidance, the cricopharyngeus is injected at two or three sites on each side, superior and lateral to the laryngectomy stoma. The cricopharyngeus is identified by electrical activity at rest that diminishes or stops when the patient swallows. The cricopharyngeus can also be injected endoscopically. Blitzer et al studied six patients who had voic e failure secondary to cricopharyngeal spasm and found that all six benefited from botulinum toxin injections, including two who had already undergone myotomies. (50) We have also found temporary benefits in a small number of patients (unpublished data, 1997 to present). Doses average 30 to 40 MU, and effects last about 3 months.

This technique is also useful for patients who have dysphagia secondary to cricopharyngeal spasm as a result of a neurologic impairment such as stroke, for those who have discoordinated swallowing, and for those who have undergone a laryngectomy. Blitzer and Brin reported improvement in six of six patients with 10 MU spread over four injection sites. (51) In another study, Annese et al compared pneumatic dilation with botulinum toxin injection in 16 patients with achalasia and elevated lower esophageal sphincter tone and found that the toxin was comparable to dilation with regard to symptom scores, even though dilation led to a significantly lower sphincter pressure. (52) There are no published studies comparing dilation and botulinum toxin in cricopharyngeal spasm.

Typically, treatment effects become evident after a few days and can last up to 5 months. No major side effects have been reported. Some patients prefer botulinum toxin injections as an alternative to myotomy or dilation. Patient selection is important and clinical trials are lacking, but this might become an indication for which botulinum toxin might prove to be very beneficial.

In conclusion, additional research--including careful documentation and the reporting of results of otolaryngologic applications of botulinum toxin--should be encouraged to help answer the remaining questions and clarify the roles of botulinum toxin in otolaryngology.

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DESCRIPTORS: **Botulinum toxin** --Therapeutic use
GEOGRAPHIC CODES/NAMES: 1USA United States
EVENT CODES/NAMES: 310 Science & research
PRODUCT/INDUSTRY NAMES: 8522200 (Medicine)
NAICS CODES: 54171 Research and Development in the Physical, Engineering, and Life Sciences

14/9/70 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01849667 SUPPLIER NUMBER: 55397051 (THIS IS THE FULL TEXT)
Minerva.(Statistical Data Included)
British Medical Journal, 319, 7203, 202
July 17,
1999
DOCUMENT TYPE: Statistical Data Included PUBLICATION FORMAT: Magazine/Journal ISSN: 0959-8146 LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 1013 LINE COUNT: 00085

TEXT:

Women doctors practising in America are a contented lot, according to an analysis of questionnaire data from the women physicians' health study (Archives of Internal Medicine 1999;159:1417-26). Despite challenges like juggling work and home, long hours, and poor control over their work, more than four fifths of a national sample reported satisfaction with their careers. Less than a third said they would not choose to do it all again.

African-Caribbean people living in the United Kingdom have a high rate of schizophrenia, twice as high African-Caribbean people living in Barbados (British Journal of **Psychiatry** 1999;175:28-33). We still don't know why this group is vulnerable to schizophrenia, but the authors of the first incidence study from Barbados reiterate the view that it may be something to do with the unexpected poverty and racism **faced** by the first immigrants 40 years ago. Unfortunately, rates of psychotic illness are getting worse with each generation.

What should happen to frozen embryos when the couples who created them divorce? An American lawyer argues that when couples disagree, the partner with the strongest case is the one who wants the embryos to be disposed of or used for research (Fertility and Sterility 1999;71:996-7). The harms of unwanted genetic reproduction, he says, outweigh the harms of losing the opportunity to reproduce with the disputed embryos. The balance only tips the other way when the embryos are a last chance at reproduction for one of the partners.

It's not often that Minerva finds a paper showing that a new treatment is actually worse than a conventional one (perhaps because they don't get published). Adding nightly lubricating ointment to a standard treatment for corneal abrasion does, however, make recurrent symptoms more likely, not less (Eye 1999;13:345-7). The authors concede that they have no randomised evidence to support their standard treatment either, but they have plans to get some.

It's not immediately clear why smoking and drinking should make gut anastamoses leaky, but retrospective analysis of data from over 300 consecutive patients in one department suggests that they do (British

Journal of Surgery 1999;86:927-31). Smokers who had colonic or rectal anastamoses were three times more likely to spring a leak than non-smokers. The risks were even higher for heavy drinkers (more than 35 units a week). A controlled trial of quitting before surgery is planned. Sometimes it's difficult to be good, but nothing could be easier (for UK readers) than telephoning 0800 55 66 96 and adding your name to a petition supporting the millennium gesture to cancel all debts owed by poor countries to rich countries. Comic Relief has organised the petition in response to a challenge from Tony Blair and Gordon Brown, who insist the British government will act if enough people want it to happen.

Wound infections are relatively rare after laparoscopic cholecystectomy, and prophylactic antibiotics don't seem to reduce the rate any further (Archives of Surgery 1999; 134:6114). A randomised trial in 450 patients found no difference in infection rates between groups given a single dose of cefotan, cefazolin, or placebo before surgery. Surgeons still using prophylaxis in straightforward elective cases should probably think again.

Amiodarone is known to cause thyroid dysfunction, and patients with congenital heart disease may be particularly vulnerable (Circulation 1999;100:149-54). In one series of 92 patients, over a third developed thyroid side effects, which were commonest in women and patients with cyanotic disease. The authors point out the irony that patients who most need the benefits of amiodarone are least able to stand the thyrotoxicosis that might follow.

Botulinum toxin is a lethal poison, but its paralysing properties make it useful for treating the anal sphincter spasm associated with anal fissure. In one trial, bilateral injections of the toxin into the internal anal sphincter worked better than twice daily applications of glyceryl trinitrate for six weeks; 96% of fissures healed in the toxin group, 60% in the glyceryl trinitrate group (New England Journal of Medicine 1999;241: 65-9) There were no relapses in either group during 15 months of follow up.

Cystoscopists in the United Kingdom don't usually decontaminate or throw away the irrigating system between patients, but a study in BJU International shows that they should (1999;83:948-53). A sensor placed in the system detected backflow of fluid from the bladder in 17% of men undergoing cystoscopy. The possibility of urine, or even blood, contaminating the connecting tubing means that endoscopy units should switch to disposable irrigating systems. The authors add a vague reassurance that it would not cost much, relative to a department's overall budget.

The role of stored iron in ischaemic heart disease is still controversial, but data from a population cohort in Rotterdam suggests that it is most important in people already at risk because of smoking, diabetes, or hypercholesterolaemia (American Journal of Clinical Nutrition 1999;69:1231-6). High serum concentrations of ferritin, the best available measure of body iron stores, were clearly linked to the risk of myocardial infarction in people with other risk factors.

The chest pain associated with achalasia of the cardia is common, unresponsive to conventional treatment, unrelated to tests of oesophageal motility and manometry, and independent of swallowing symptoms, say two German researchers who have been following up their patients since 1981 (Gastroenterology 1999;116:1300-4). Nearly two thirds of their new patients had episodic chest pain, which tended to occur early in the course of the disease and to improve with age.

Deaths from cardiovascular disease in the Netherlands have fallen by about 2% a year since 1975. The cloud to this silver lining is that the survivors have contributed to a relentless and expensive rise in hospital admissions for heart failure, chronic coronary syndromes, and diseased arteries (Heart 1999;82:52-6). Worse, the lifetime chance of dying a cardiovascular death is still 40%.

DESCRIPTORS: Cardiovascular diseases--Mortality; **Botulinum toxin** -- Therapeutic use
FILE SEGMENT: HI File 149

SPECIAL FEATURES: table; illustration
DESCRIPTORS: **Botulinum toxin** --Therapeutic use; Strabismus--Care and treatment; Muscle contraction--Abnormalities; Dystonia--Care and treatment
FILE SEGMENT: HI File 149

14/9/72 (Item 5 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01373548 SUPPLIER NUMBER: 13222810 (THIS IS THE FULL TEXT)
Botulinum toxin: useful in adult onset focal dystonias. (Editorial)
Lees, A.J.
British Medical Journal, v305, n6863, p1169(2)
Nov 14,
1992
DOCUMENT TYPE: Editorial PUBLICATION FORMAT: Magazine/Journal ISSN: 0959-8146 LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 1051 LINE COUNT: 00113

TEXT:

Human botulism, due to the ingestion of toxin produced by Clostridium botulinum, is rare but potentially fatal and causes an acute symmetric descending paralytic illness particularly affecting eye and bulbar muscles.[1] The toxin paralyses by preventing the release of acetylcholine from nerve terminals --thereby leading to irreversible neuromuscular blockade. Recovery occurs over about three months as axons resprout and new extrajunctional acetylcholine receptors form. Although antitoxins and antibiotics are recommended, there is no known cure.

Botulinum toxin was first used therapeutically to correct squints by altering the balance between muscles responsible for the abnormal position of the eye in the orbit.[2] Since then it has become the preferred treatment for several adult onset focal dystonias and hemifacial spasm. Indications for its use increase rapidly, and its role is currently being explored in various medical and surgical specialties. The specific local effects of injections with botulinum toxin in inducing temporary muscle weakness have already helped thousands of patients with previously untreatable, often painful, and functionally devastating muscle spasms. Not surprisingly, introduction of this treatment into clinical practice has also stimulated a flurry of sensational media publicity, with headlines ranging from "a little bit of botulinum can do you good" to "lethal nerve poison miraculously makes the blind see and the mute speak."

In the focal dystonias, a poorly understood group of conditions believed to be due to neurochemical abnormalities in the basal ganglia, treatment has been based on the injection of small quantities of botulinum toxin into the locally affected muscles to produce weakness sufficient to eliminate excessive contraction at the same time as preserving function. The clinical effect appears between one and 15 days after injection and in most cases wears off completely between four and 16 weeks. Essential blepharospasm, which usually begins after the fourth decade of life and is characterised by involuntary repetitive closure of the eyelids, leading to impaired visual function, responds extremely well. Botulinum toxin is injected into three or four superficial sites in each orbicularis oculi muscle, and worthwhile temporary improvement occurs in four out of five patients.[3] Pretarsal forms of blepharospasm and apraxia of eyelid opening do not respond well. Focal brusing and transient partial ptosis are relatively common whereas transient diplopia and mild facial weakness are rare adverse reactions.

Patients with blepharospasm continue to be misdiagnosed as having a primary **psychiatric** illness, which leads to inappropriate, distressing referral, and some may have developed their dystonia from inappropriate long term administration of neuroleptic drugs (such as antipsychotics, metoclopramide, and prochlorperazine). Some patients have additional lower

facial and jaw opening and closing spasms, which may also respond to botulinum toxin, although the results are less good.

Hemifacial spasm due to intermittent synchronous contraction of the ipsilateral facial nerve is another established indication for botulinum toxin. Other drug treatment is ineffective, and the morbidity and unpredictable results of the current recommended neurosurgical approaches are a major drawback. In hemifacial spasm the muscle contractions usually begin around one orbicularis oculi muscle and then spread to affect the brow, lower **face** , and platysma. Unlike blepharospasm, the movements are invariably unilateral and may continue in sleep. Chewing and talking characteristically aggravate hemifacial spasm; in contrast, blepharospasm is exacerbated by bright light, reading, or watching television. Injection into the affected orbicularis oculi muscle removes the eye spasm in over 90% of cases, and a further single small injection into the corrugator muscle may also help mid- **face** spasm.[4] Together with congenital and acquired squints (particularly those that in turn) blepharospasm and hemifacial spasm constitute the only licensed indications for botulinum type A toxin in the United Kingdom.

Spasmodic toricollis--like blepharospasm, another adult onset focal dystonia--also responds well to botulinum toxin, and many neurologists now regard this as the preferred treatment. The condition usually presents in middle age with involuntary torsion or jerky movements of the neck, frequently accompanied by pain and crippling depression. Because of the complexity of the neck musculature the overall results are less good than those after injection into the orbicularis oculi muscle, but neck posture improves by at least 70% with an even greater improvement in pain relief.[5-7] The simple rotatory forms involving mainly the sternomastoid on one side and the contralateral posterior cervical muscles do best. Mild neck weakness and transient dysphagia are the commonest side effects. A few patients go into spontaneous remission during long term treatment whereas about 5% become refractory to serial injections after two or three years.

Other highly promising uses for botulinum toxin are in the treatment of laryngeal dystonia[8] and hand cramps, including writers' and musicians' dystonias, golfers' "yips," and dart players' cramp.[9 10] The toxin may also have a role in treating severe spasticity, facilitating physiotherapy by temporarily relieving pain and increased muscle tone, and in dystonic foot cramps. More controversial uses include pain relief in sports injuries and chronic tension headaches, alleviating eye wrinkles in cosmetic surgery, and injecting the puborectalis muscle to treat a special form of constipation anismus. The toxin has also been used to treat palatal myoclonus, stridor, urinary symptoms, and dysthyroid eye disease.

Treatment with botulinum type A toxin has provided welcome relief and hope for patients with adult onset focal dystonias, who may number 30 000 in the United Kingdom. Despite its drawbacks, which include the need to repeat the injection three or four times a year and its expense (about 100 [Pounds] per injection for blepharospasm and 300 [Pounds] for torticollis), it has become an established treatment in ophthalmological and neurological practice.[11] Patients have continued to respond with benefit for more than five years, although antibodies to the toxin may develop in the peripheral blood, leading to initial unresponsiveness or late resistance.[12] Long term effects on muscle function both locally and distant form the site of injection have yet to be determined. Trials of other types of botulinum toxin are under way, and more effective toxins capable of producing longer durations of benefit without inevitably increasing unwanted effects may be developed in the near future.

1 Hutchinson DN. Foodborne botulism. BM[unkeyable] 1992;305:262-5.

2 Scott AB. Botulinum toxin injections into extraocular muscles as an alternative to strabismus surgery. Ophthalmology 1980;87:1044-9.

3 Elston JS, Russell RWR. Effect of treatment with botulinum toxin on neurogenic blepharospasm. BM[unkeyable] 1985;290:1857-9.

4 Elston JS. Botulinum toxin treatment of hemifacial spasm. [unkeyable] Neurol Neurosurg **Psychiatry** 1986;49:827-9.

5 Tsui JKC, Eisen A, Stoessi AJ, Calne S, Calne DB. Double-blind study of botulinum toxin in spasmodic torticollis. Lancet 1986;ii:245-6.

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7 Blackie JD, Lees AJ, Botulinum toxin in the treatment of spasmodic

torticollis. [unkeyable] Neurol Neurosurg **Psychiatry** 1990;53:640-3.
8 Brian MF, Blitzer A, Fahn S, Gould W, Lovelace RE. Adductor laryngeal dystonia (spastic dysphonia): treatment with local injections of botulinum toxin. Mov Disord 1989;4:287-96.
9 Cohen LG, Hallett M, Geller BD, Hochberg F. Treatment of focal dystonias of the hand with botulinum toxin injections. [unkeyable] Neurol Neurosurg **Psychiatry** 1989;52:355-63.
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11 American Academy of Neurology. Assessment: the clinical usefulness of botulinum toxin-A in treating neurologic disorders. Neurology 1990;40:1332-6.
12 Hambleton P, Cohen HE, Palmer BJ, Melling J. Antitoxins and botulinum toxin treatment. BM[unkeyable] 1992;304:950-60.

DESCRIPTORS: **Botulinum toxin** --Therapeutic use; Dystonia--Drug therapy
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        (c) 2005 American Chemical Society
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        (c) 2005 Mass. Med. Soc.
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4/9/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

17540805 PMID: 15540518
Systemic lupus erythematosus in Pakistan.
Rabbani M A; Siddiqui B K; Tahir M H; Ahmad B; Shamim A; Shah S M A; Ahmad A
Department of Medicine, The Aga Khan University Hospital, Karachi, Pakistan. anasrabbani@yahoo.com
Lupus (England) 2004, 13 (10) p820-5, ISSN 0961-2033
Journal Code: 9204265
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS
Clinical features of systemic lupus erythematosus (SLE) have been described from different geographical regions in the world, with some clinical differences among different racial groups. Although data on the characteristics of SLE in Pakistan is scarce, it is not uncommon in the South East Asian region. The purpose of this study was, therefore, to delineate the clinical pattern and disease course in Pakistani patients with SLE and to compare it with international data on lupus patients. A total of 196 patients with SLE fulfilling the clinical and laboratory criteria of the American Rheumatism Association admitted to the hospital between 1986 and 2001 were studied by means of a retrospective **review** of their records. Demographically, it was seen that SLE is a disease predominantly of females in their third decade, which is consistent with worldwide data. The mean age of presentation was 31 years (range 14-76) and the mean duration of follow up was 34 (4-179) months. Generally, there was less cutaneous (46%), arthritic (38%), serositis (22%) and renal involvement (33%) but more **neuropsychiatric symptoms** (26%) in our population. Eighty-six percent of patients were ANA positive, whereas anti dsDNA was positive in 74% of patients. Infections, renal involvement, seizures and thrombocytopenia were associated with poor prognosis ($P < 0.05$). This study is the first of its kind in Pakistan. The clinical and laboratory characteristics of SLE patients in our study place our population in the middle of a spectrum between the Caucasians and other Asian populations. It has shown that the clinical characteristics of SLE patients in this country may be different to those of its neighbors.
Record Date Created: 20041115

4/9/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

17426174 PMID: 15355758
Neurosurgical interventions for neuropsychiatric syndromes.
Anderson C Alan; Arciniegas David B
Neurology B-182, University of Colorado Health Sciences Center, 4200 East Ninth Avenue, Denver, CO 80262, USA. al.anderson@uchsc.edu
Current psychiatry reports (United States) Oct 2004, 6 (5) p355-63, ISSN 1523-3812 Journal Code: 100888960
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS
Psychosurgical procedures have been used for the treatment of intractable mental illness for more than 50 years. With improvements in surgical techniques, including new implantable stimulators, advances in functional neuroimaging, and progress in our fundamental understanding of the pathophysiology of mental illness there is a renewed interest in

neurosurgical treatment of refractory psychiatric illness. This article will **review** the history of psychosurgery and recent developments in surgical techniques and implantable devices used in this context. The results of psychosurgery for the treatment of several psychiatric conditions and **neuropsychiatric symptoms** will be presented, including obsessive-compulsive disorder, Tourette's syndrome, depression, anxiety, aggression, self-injurious behavior, and schizophrenia. Lastly, a perspective on the current and future role of psychosurgery for the treatment of mental illnesses will be discussed.
Record Date Created: 20040909

4/9/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

17473284 PMID: 15488246
The phenomenology and treatment of interferon-induced depression.
Loftis Jennifer M; Hauser Peter
Behavioral Health and Clinical Neurosciences Division, Portland VA Medical Center, Portland, OR, USA. loftisj@ohsu.edu
Journal of affective disorders (Netherlands) Oct 15 2004, 82 (2) p175-90, ISSN 0165-0327 Journal Code: 7906073
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS
Interferon (IFN)-alpha, IFN-beta, and IFN-gamma are currently available for the treatment of malignancies, viral infections (e.g., hepatitis C virus), multiple sclerosis (MS), and skin conditions. In addition to their therapeutic effects, IFNs commonly cause various side effects. Most common among the side effects of IFN are "flu-like" **symptoms** such as chills, fever, and muscle soreness. However, IFN can also cause significant **neuropsychiatric** side effects, particularly **symptoms** of depression. A literature search was conducted in order to summarize current information on (1) the frequency, characteristics, and risk factors of IFN-induced depression, (2) possible biochemical mechanisms associated with IFN-induced depression, and (3) the treatment strategies for IFN-induced depression. **Review** of the literature suggests that **symptoms** of depression induced by IFN therapy, in particular IFN-alpha therapy, are common and can limit the treatment utility, often necessitating discontinuation of IFN therapy or the use of psychopharmacologic agents. Depression is also a suspected side effect of therapy with IFN-beta and IFN-gamma; however, the association has not been as convincingly confirmed. Importantly, IFNs affect neurochemical pathways putatively involved in the etiology of depression. While these depressive side effects usually resolve after the completion of IFN therapy, they can persist or reappear with dose escalations. It is recommended that health care providers, patients and their families be informed about the potential risk of the psychiatric disturbances that can occur with IFN-alpha therapy. Screening and monitoring, ideally using **symptom** rating scales for depression, and early antidepressant treatment intervention appear necessary to optimize IFN therapy for the majority of patients.
Record Date Created: 20041018

4/9/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

16895999 PMID: 15181787
[Typical benign epilepsy potentials in childhood (Rolandic spikes)--neurobiological and neuropsychological symptoms **and their clinical significance in child and adolescent psychiatry]**
Benigne epilepsietypische Potentiale des Kindesalters (Rolando-Spikes)--n

eurobiologische und neuropsychologische Befunde und ihre klinische Bedeutung in der Kinder- und Jugendpsychiatrie.
Holtmann M; Becker K; el-Faddagh M; Schmidt M H
Klinik fur Psychiatrie und Psychotherapie des Kindes- und Jugendalters, Klinikum der Johann Wolfgang Goethe-Universitat, Frankfurt. holtmann@em.uni-frankfurt.de
Zeitschrift fur Kinder- und Jugendpsychiatrie und Psychotherapie (Switzerland) May 2004, 32 (2) p117-29, ISSN 1422-4917
Journal Code: 9801717
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
INTRODUCTION: Rolandic epilepsy is the most frequent epileptic syndrome in childhood, electroencephalographically characterized by focal sharp waves, so called rolandic spikes (benign epileptiform discharges of childhood). These discharges occur in about 1.5 to 2.4% of children; only 10% of them suffer from epileptic seizures. METHODS: This paper **reviews** genetic, epidemiological, radiological, neurophysiologic, metabolic and neuropsychological findings in children with rolandic discharges. RESULTS: The epileptologic course is favorable, seizures and EEG features usually resolve completely at puberty. In contrast to former assumptions, **symptoms** range from infrequent seizures to neuropsychological deficits and behavior problems, even in children without overt seizures. The impact of rolandic spikes on the development of affected children and their behavior is unclear. Two models try to elucidate the relation between EEG discharges and neuropsychological disorders. The first regards neuropsychological disturbances as transient cognitive impairment due to epileptiform discharges; the second model strengthens the role of a hereditary impairment of brain maturation. CONCLUSIONS: The benefit of pharmacotherapy for treating **neuropsychiatric symptoms** in children with rolandic spikes but without overt seizures remains to be clarified. (80 Refs.)
Tags: Human
Descriptors: *Cerebral Cortex--physiopathology--PP; *Electroencephalography; *Epilepsy, Rolandic--genetics--GE; *Neuropsychological Tests; Adolescent; Child; Child Behavior Disorders--diagnosis--DI; Child Behavior Disorders--genetics--GE; Child Behavior Disorders--physiopathology--PP; Child Behavior Disorders--psychology--PX; Child, Preschool; Epilepsy, Rolandic--diagnosis--DI; Epilepsy, Rolandic--physiopathology--PP; Epilepsy, Rolandic--psychology--PX; Evoked Potentials--physiology--PH; Genetic Predisposition to Disease--genetics--GE; Infant; Language Development Disorders--diagnosis--DI; Language Development Disorders --genetics--GE; Language Development Disorders--physiopathology--PP; Language Development Disorders--psychology--PX; Learning Disorders --diagnosis--DI; Learning Disorders--genetics--GE; Learning Disorders --physiopathology--PP; Learning Disorders--psychology--PX; Phenotype; Prognosis; Risk; Twin Studies
Record Date Created: 20040608
Record Date Completed: 20040916

4/9/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

16802471 PMID: 15291655
Motor **conversion disorders** reviewed **from a** neuropsychiatric **perspective.**
Krem Maxwell M
Department of Internal Medicine, Washington University School of Medicine, St. Louis, MO 63110, USA. mkrem@im.wustl.edu
Journal of clinical psychiatry (United States) Jun 2004, 65 (6) p783-90, ISSN 0160-6689 Journal Code: 7801243
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

BACKGROUND: Conversion disorder is a somatoform disorder defined by the presence of pseudoneurologic **symptoms** relating to voluntary sensory or motor function. The correct diagnosis of conversion disorder presenting with motor **symptoms** is complicated by the lack of gold-standard diagnostic tests and the absence of a universally accepted set of positive diagnostic criteria. This article **reviews** the epidemiology, pathophysiology, presentation, differential diagnosis, treatment, and prognosis of motor conversion, placing emphasis on diagnostic validity, reliability, and utility, while evaluating the empirical evidence supporting diagnostic and treatment strategies. DATA SOURCES AND STUDY SELECTION: Literature searches were carried out in PubMed using the keywords conversion disorder, motor conversion, dystonia, psychogenic, hysteria, somatization, motion disorder, movement disorder, and patho-physiology. Articles and book chapters in the author's personal collection were also utilized. CONCLUSIONS: Advances in neuropsychiatric research are leading to significant improvements in the diagnosis and understanding of motor conversion disorders. Positive, objective, and quantitative diagnostic criteria show significant promise for enhancing diagnostic accuracy. Current pathophysiologic research has begun to provide mechanistic explanations for conversion **symptoms** , thus blurring the distinction between psychogenic and organic motor disorders. (82 Refs.)

Tags: Human

Descriptors: *Conversion Disorder--diagnosis--DI; *Movement Disorders --diagnosis--DI; Cerebral Cortex--physiopathology--PP; Conversion Disorder --physiopathology--PP; Conversion Disorder--therapy--TH; Diagnosis, Differential; Dystonia--diagnosis--DI; Dystonia--therapy--TH; Electric Stimulation Therapy--methods--MT; Electroconvulsive Therapy--methods--MT; Laterality--physiology--PH; Magnetic Resonance Imaging; Movement Disorders --physiopathology--PP; Movement Disorders--therapy--TH; Muscle Weakness --diagnosis--DI; Muscle Weakness--physiopathology--PP; Muscle Weakness --therapy--TH; Prognosis; Psychophysiologic Disorders--diagnosis--DI; Psychophysiologic Disorders--physiopathology--PP; Psychophysiologic Disorders--therapy--TH; Psychotherapy--methods--MT; Psychotropic Drugs --therapeutic use--TU; Somatoform Disorders--diagnosis--DI; Somatoform Disorders--physiopathology--PP; Somatoform Disorders--therapy--TH; Tomography, Emission-Computed

CAS Registry No.: 0 (Psychotropic Drugs)
Record Date Created: 20040804
Record Date Completed: 20040831

4/9/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

16149240 PMID: 15060240

The pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) etiology for tics and obsessive-compulsive symptoms : hypothesis or entity? Practical considerations for the clinician.

Kurlan Roger; Kaplan Edward L
Cognitive and Behavioral Neurology Unit, Department of Neurology, University of Rochester School of Medicine, Rochester, New York 14642-8673, USA. roger kurlan@urmc.rochester.edu

Pediatrics (United States) Apr 2004, 113 (4) p883-6, ISSN 1098-4275 Journal Code: 0376422
Contract/Grant No.: NS42240; NS; NINDS
Comment in Pediatrics. 2004 Apr;113(4) 907-11; Comment in PMID 15060242
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

Clinicians have been faced with much publicity and contradictory

scientific evidence regarding a recently described condition termed pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS). It has been proposed that children with PANDAS experience tics, obsessive-compulsive **behavior** , and perhaps other **neuropsychiatric symptoms** as an autoimmune response to streptococcal infection. We **review** current scientific information and conclude that PANDAS remains a yet-unproven hypothesis. Until more definitive scientific proof is forthcoming, there seems to be insufficient evidence to support 1) routine microbiologic or serologic testing for group A streptococcus in children who present with **neuropsychiatric symptoms** or 2) the clinical use of antibiotic or immune-modifying therapies in such patients. The optimum diagnostic and therapeutic approach awaits the results of additional research studies.

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: *Autoimmune Diseases--etiology--ET; *Obsessive-Compulsive Disorder--immunology--IM; *Streptococcal Infections--complications--CO; *Streptococcus pyogenes; *Tic Disorders--immunology--IM; Adjuvants, Immunologic--therapeutic use--TU; Adolescent; Age of Onset; Anti-Bacterial Agents--therapeutic use--TU; Child; Child, Preschool; Obsessive-Compulsive Disorder--drug therapy--DT; Obsessive-Compulsive Disorder--etiology--ET; Streptococcal Infections--diagnosis--DI; Streptococcal Infections --prevention and control--PC; Streptococcus pyogenes --isolation and purification--IP; Tic Disorders--drug therapy--DT; Tic Disorders--etiology --ET

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Anti-Bacterial Agents)

Record Date Created: 20040402

Record Date Completed: 20040513

4/9/25 (Item 25 from file: 155)

16008085 PMID: 14754384

Acetylcholinesterase inhibition in Alzheimer's Disease.

Ibach Bernd; Haen Ekkehard

Memory Disorders Clinic, Gerontopsychiatric and Clinical Pharmacology Research Unit, Department of Psychiatry, University of Regensburg, Bezirksklinikum Regensburg, Germany. bernd.ibach@bzk.uni-regensburg.de

Current pharmaceutical design (Netherlands) 2004, 10 (3) p231-51, ISSN 1381-6128 Journal Code: 9602487

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Alzheimer's Disease (AD) is the most common cause for dementia in our ageing population, which leads to a slowly progressive, irretrievable ruination of mental function. The destructive, primarily degenerative condition is neuropathologically characterized by the formation of amyloid plaques, neurofibrillary tangles and loss of neurons and synapses as well. Research during the past twenty years revealed early in the disease course a degeneration of cholinergic nuclei localised in the basal forebrain. Impairment of this cholinergic system, which projects into large areas of the limbic system and the neocortex is followed by disturbance of attentional processes and cognitive decline. The link between the cholinergic dysfunction and cognitive impairment has focused large scientific efforts to understand the neurobiology of cognition and to develop therapeutic tools for the fight against Alzheimer's Disease. Acetylcholinesterase inhibitors are currently the best established treatment for this devastating disease. This **review** describes historical aspects and the vast range of use of cholinesterase inhibitors in traditional societies and industrial nations. Second, the rational basis will be outlined for their development as medication, the so-called cholinergic hypotheses of AD. Third, acetylcholinesterase inhibitors currently available for the treatment of AD will be **reviewed** . This

disease. **Neuropsychiatric** and cognitive adverse events occur more frequently on anticholinergics than on placebo and are a...

...measures are conflicting and data do not strongly support a differential clinical effect on individual **parkinsonian** features. Data is insufficient to allow comparisons in efficacy or tolerability between individual anticholinergic drugs.
Descriptors: *Cholinergic Antagonists--therapeutic use--TU; * **Parkinson** Disease--drug therapy--DT

5/6,KWIC/20 (Item 20 from file: 155)

12340612 PMID: 12707840
Dementia with lewy bodies--diagnosis and treatment.
Mar 8 2003

... neurofibrillary tangles. Core clinical features are fluctuating cognitive impairment, persistent visual hallucinations and extrapyramidal motor **symptoms** (**parkinsonism**). One of these core features has to be present for a diagnosis of possible DLB...

... DLB is clinically under-diagnosed and frequently misclassified as systemic delirium or dementia due to **Alzheimer** 's disease or cerebrovascular disease. Therapeutic approaches to DLB can pose difficult dilemmas in pharmacological...

... is associated with increased morbidity and mortality. Antiparkinsonian medication has the potential to exacerbate psychotic **symptoms** and may be relatively ineffective at relieving extrapyramidal motor **symptoms** . Recently there is converging evidence that treatment with cholinesterase inhibitors can offer a safe alternative for the **symptomatic** treatment of cognitive and **neuropsychiatric** features in DLB. This **review** will focus on the clinical characteristics of DLB, its differential diagnosis and on possible management...

5/6,KWIC/21 (Item 21 from file: 155)

12282690 PMID: 12636182
A clinical overview of cholinesterase inhibitors in Alzheimer **'s disease.**
2002

A clinical overview of cholinesterase inhibitors in Alzheimer **'s disease.**
This **review** provides an overview of the three most widely used cholinesterase (ChE) inhibitors: donepezil, rivastigmine, and...

... and tolerability of the various agents. In addition to providing cognitive benefits in patients with **Alzheimer** 's disease (AD), growing clinical evidence also suggests that ChE inhibitors can produce favorable and clinically relevant effects on **neuropsychiatric** / **behavioral** disturbances and activities of daily living. Furthermore, recent data indicate that these agents may be...

... wider spectrum of dementias which share a common cholinergic deficit, such as Lewy body dementia, **Parkinson** 's disease dementia, and vascular dementia, is currently under investigation. Beyond **symptomatic** relief, data suggest that ChE inhibitors may also slow the underlying disease process. As clinical...
Descriptors: ***Alzheime*** r Disease--drug therapy--DT; *Cholinesterase Inhibitors--administration and dosage--AD; Aged; **Alzheimer** Disease--blood --BL; **Alzheimer** Disease--psychology--PX; Carbamates--administration and dosage--AD; Carbamates--adverse effects--AE; Carbamates--pharmacokinetics

--PK...

5/6,KWIC/22 (Item 22 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

12182597 PMID: 12517232
Efficacy of cholinesterase inhibitors in the treatment of neuropsychiatric symptoms **and functional impairment in** Alzheimer **disease: a meta-analysis.**
Jan 8 2003

Efficacy of cholinesterase inhibitors in the treatment of neuropsychiatric symptoms **and functional impairment in** Alzheimer **disease: a meta-analysis.**
CONTEXT: Cholinesterase inhibitors are the primary treatment for the cognitive **symptoms** of **Alzheimer** disease (AD). Cholinergic dysfunction is also associated with **neuropsychiatric** and functional deficits, but results from randomized controlled trials of cholinesterase inhibitors are conflicting. OBJECTIVE: To conduct a systematic **review** and meta-analysis to quantify the efficacy of cholinesterase inhibitors for neuropsychiatric and functional outcomes...

... and the Cochrane Controlled Trials Register. We retrieved English- and non-English-language articles for **review** and collected references from bibliographies of **reviews** , original research articles, and other articles of interest. We searched for both published and unpublished...
... outcomes. Neuropsychiatric outcomes were measured with the Neuropsychiatric Inventory (NPI, 0-120 points) and the **Alzheimer** Disease Assessment Scale, noncognitive (ADAS-noncog, 0-50 points) and were analyzed with the weighted...
Descriptors: ***Alzheime** r Disease--drug therapy--DT; *Cholinesterase Inhibitors--therapeutic use--TU; Activities of Daily Living; **Alzheimer** Disease--physiopathology--PP; Neuropsychological Tests; Treatment Outcome

5/6,KWIC/23 (Item 23 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

12122862 PMID: 12453674
Mood stabilizers in Alzheimer **'s disease:** symptomatic **and neuroprotective rationales.**
Dec 7 2002

Mood stabilizers in Alzheimer **'s disease:** symptomatic **and neuroprotective rationales.**
... case study of 'reverse translational research', in which empirical clinical trials focused on relieving psychopathological **symptoms** of **Alzheimer** 's disease (AD) ultimately led to mechanism-based trials addressing aspects of the underlying pathophysiology of **Alzheimer** 's disease. AD is multi-dimensional in nature, characterized not only by cognitive and functional decline but by **neuropsychiatric symptoms** that develop commonly and are associated with considerable morbidity. There have been a large number of empirical trials of various pharmacological agents to reduce these **symptoms** , such as agitation. Although antipsychotics are used most frequently for agitation, the usual effect size...

... to delay or prevent the emergence of psychopathology. FINDINGS: The evidence of clinical trials is **reviewed** regarding the safety, tolerability, and apparent efficacy of the mood stabilizers carbamazepine and valproate for agitation associated with AD. Possible mechanisms of action of valproate are **reviewed** , leading to the surprising conclusion that neuroprotective properties may account for some of its clinical...

... valproate therapy can attenuate the clinical progression of AD, which will be implemented by the **Alzheimer** 's Disease Cooperative Study. The design addresses valproate's potential to delay or prevent the...

Descriptors: ***Alzheime*** r Disease--drug therapy--DT; * **Alzheimer** Disease--psychology--PX; *Neuroprotective Agents--therapeutic use--TU; **Alzheimer** Disease--metabolism--ME; Animals; Clinical Trials--methods--MT; Mood Disorders--drug therapy--DT; Mood Disorders...

5/6,KWIC/24 (Item 24 from file: 155)

12023918 PMID: 12243634
Prevalence of neuropsychiatric symptoms **in dementia and mild cognitive impairment: results from the cardiovascular health study.**
Sep 25 2002

Prevalence of neuropsychiatric symptoms **in dementia and mild cognitive impairment: results from the cardiovascular health study.**
... a precursor to dementia, at least in some cases. Dementia and MCI are associated with **neuropsychiatric symptoms** in clinical samples. Only 2 population-based studies exist of the prevalence of these **symptoms** in dementia, and none exist for MCI. OBJECTIVE: To estimate the prevalence of **neuropsychiatric symptoms** in dementia and MCI in a population-based study. DESIGN: Cross-sectional study derived from...

... 4 US counties. Dementia and MCI were classified using clinical criteria and adjudicated by committee **review** by expert neurologists and psychiatrists. A total of 824 individuals completed the Neuropsychiatric Inventory (NPI...

...and 142 did not meet criteria for MCI or dementia. MAIN OUTCOME MEASURE: Prevalence of **neuropsychiatric symptoms** , based on ratings on the NPI in the previous month and from the onset of cognitive **symptoms** . RESULTS: Of the 682 individuals with dementia or MCI, 43% of MCI participants (n = 138) exhibited **neuropsychiatric symptoms** in the previous month (29% rated as clinically significant) with depression (20%), apathy (15%), and irritability (15%) being most common. Among the dementia participants, 75% (n = 270) had exhibited a **neuropsychiatric symptom** in the past month (62% were clinically significant); 55% (n = 199) reported 2 or more...

... participants (n = 233) and 50% of MCI participants (n = 139) exhibited at least 1 NPI **symptom** from the onset of cognitive **symptoms** . There were no differences in prevalence of **neuropsychiatric symptoms** between participants with **Alzheimer** -type dementia and those with other dementias, with the exception of aberrant motor behavior, which was more frequent in **Alzheimer** -type dementia (5.4% vs 1%; P =.02). CONCLUSIONS: **Neuropsychiatric symptoms** occur in the majority of persons with dementia over the course of the disease. These are the first population-based estimates for **neuropsychiatric symptoms** in MCI, indicating a high prevalence associated with this condition as well. These **symptoms** have serious adverse consequences and should be inquired about and treated as necessary. Study of **neuropsychiatric symptoms** in the context of dementia may improve our understanding of brain-behavior relationships.
Descriptors: *Anxiety; *Behavioral **Symptoms** --epidemiology--EP; *Cognition Disorders--epidemiology--EP; *Cognition Disorders--psychology --PX; *Dementia--epidemiology--EP; *Dementia--psychology...

5/6,KWIC/25 (Item 25 from file: 155)

11946759 PMID: 12151841
Neuropsychiatric symptoms **in the dementias.**
Aug 2002

Neuropsychiatric symptoms **in the dementias.**
PURPOSE OF **REVIEW** : **Neuropsychiatric** , or non-cognitive **symptoms** are increasingly recognized as manifestations of dementias. RECENT FINDINGS: In

Alzheimer 's disease, recent advances have included the identification of behavioral profiles, differentiation of apathy and...

... factors for psychosis and its links to agitation and aggression, and an analysis of depressive **symptoms** in the absence of major depression. Functional neuroimaging data mainly supported the role of the...

... and particularly aberrant social behavior. The frequency of delusions and visual hallucinations was increased in **Parkinson** 's disease, **Parkinson** 's disease with dementia, and dementia with Lewy bodies, suggesting common mechanisms such as Lewy body pathology and cholinergic deficiency. The latter was supported by an improvement of these **symptoms** by cholinesterase inhibitors. SUMMARY: Future research directions include both clinical and basic neuroscience investigations. The detection of early **neuropsychiatric symptoms** might be a marker for dementia, and the possible existence of a mild neuropsychiatric impairment syndrome should be explored. More longitudinal studies with pathological confirmation will facilitate correlations with **neuropsychiatric symptoms** . Functional neuroimaging and **behavioral** neurogenetics will permit in-vivo correlations and consequently help patient management and care.

Descriptors: ***Alzheime*** r Disease--diagnosis--DI; * **Alzheimer** Disease --psychology--PX; *Depression--diagnosis--DI; *Psychotic Disorders --diagnosis--DI

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Set     Items   Description
S1       7104   NEUROPSYCHIAT? (10N) (SYMPTOM? OR BEHAVIOR? OR MOTOR? OR P-
             HYSICAL?)
S2    5930254   REVIEW? OR TUTOR?
S3       1457   S1 AND S2
S4       1144   S3 AND SYMPTOM?
S5        456   S4 AND (EPILEPSY? OR PARKINSON? OR FIBROMYAL? OR PAIN? OR -
             MIGRANE? OR HEADACHE? OR ALZHEIMER?)
S6        318   S1 AND (MIGRANE? OR HEADACHE?)
S7          0   S6 AND MIGRANE?
S8        117   'MIGRAINE'
S9      87415   MIGRAINE?
S10        57   S1 AND (S8 OR S9)
?t s10/9/4 5 6
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10/9/4 (Item 4 from file: 155)

12158153 PMID: 12491066

[Neuropsychiatric involvement in systemic lupus erythematosus. Part 1: clinical presentation and pathogenesis]

Neuropsychiatrische beteiligung des systemischen lupus erythematodes. Teil 1: klinik und pathogenese.

Weiner Stefan Markus; Peter Hans Hartmut

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Medizinische Klinik (Munich, Germany - 1983) (Germany) Dec 15 2002, 97 (12) p730-7, ISSN 0723-5003 Journal Code: 8303501

Document type: Journal Article; Review; Review Literature ; English Abstract

Languages: GERMAN

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

BACKGROUND: Central nervous system (CNS) involvement is a frequent complication of systemic lupus erythematosus (SLE) ranging from a subclinical to a severe disabling disease. Neuropsychiatric manifestations have been described in 18-67% of cases depending on the diagnostic criteria. The cerebral involvement may precede the full-blown picture of SLE or may develop in the course of disease, most frequently within the first 3 years. CLINICAL PRESENTATION: **Neuropsychiatric** manifestations in SLE comprise diffuse psychiatric **symptoms** , focal neurologic **symptoms** , and the involvement of the peripheral nervous system. Numerous CNS syndroms have been described: **migraine** , seizure, stroke, chorea, transverse myelopathy, psychosis, mood disorders, acute confusional state, and cognitive dysfunction. The diagnosis of cerebral involvement can be difficult and has to be differentiated from neurologic complications which may be, for instance, due to uremia, hypertension, drug toxicity, and infection. PATHOGENESIS: A large number of etiopathophysiologic processes are involved: antineuronal antibodies, antibodies against ribosimal P-protein, and cytokines have been implicated in the pathogenesis of diffuse **neuropsychiatric symptoms** . Focal neurologic **symptoms** are the consequence of vascular injury induced by circulating immune complex, occlusive vasculopathy as a result of endothelial cell activation induced by cytokines and complement activation, or macro- and microvascular thrombosis induced by antiphospholipid antibodies. In the later stages of disease, cerebrovascular manifestations are often related to accelerated atherosclerosis, which is entertained by increased intravascular complement turnover and antiphospholipid antibodies. (96 Refs.)

Tags: Human

Descriptors: *Lupus Erythematosus, Systemic--diagnosis--DI; *Lupus Vasculitis, Central Nervous System--diagnosis--DI; Diagnosis, Differential; Neurologic Examination; Neuropsychological Tests; Peripheral Nervous System Diseases--diagnosis--DI; Prognosis

Record Date Created: 20021219

Record Date Completed: 20030417

10/9/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08849392 PMID: 1901447

Autoantibodies and rheumatic disorders in a neurology inpatient population: a prospective study.

Olsen M L; O'Connor S; Arnett F C; Rosenbaum D; Grotta J C; Warner N B
Department of Internal Medicine, University of Texas Health Science Center, Houston 77225.

American journal of medicine (UNITED STATES) Apr 1991, 90 (4) p479-88, ISSN 0002-9343 Journal Code: 0267200
Contract/Grant No.: M01-RR-02558; RR; NCRR
Comment in Am J Med. 1992 Mar;92(3) 341; Comment in PMID 1546737
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

PURPOSE: To determine the prevalence and spectrum of underlying rheumatic diseases, especially Sjogren's syndrome (SS) and the antiphospholipid syndrome, and the prevalence of the lupus anticoagulant, antinuclear antibody (ANA), and rheumatoid factor (RF) within a neurologic patient population. PATIENTS AND METHODS: The study design entailed a prospective, consecutive sample of patients admitted to a university-affiliated neurology service for 72 hours or more. Study patients were obtained from a sequential evaluation of 100 inpatients with a wide spectrum of neurologic diseases. Another 31 eligible patients were not included due to refusal (n = 4), inability to give consent (n = 12), or an incomplete database (n = 15). All patients underwent a physical examination and responded to a rheumatic disease questionnaire (administered by one rheumatologist) assessing signs and symptoms relevant to rheumatic disease. All had lupus anticoagulant, ANA, and RF determinations. An independent patient evaluation was done by the attending neurologist. RESULTS: Eleven patients had a rheumatic or autoimmune disorder directly related to their neurologic admission: three patients with SS (one each with embolic stroke, dementia, and hemiparetic somatization); three patients with lupus anticoagulant syndrome (all with stroke, recurrent in two); one patient with systemic lupus erythematosus accompanied by **migraine** headache and the lupus anticoagulant; and one patient each with isolated central nervous system (CNS) angiitis, neuro-Behcet's disease, CNS Whipple's disease, and HLA-B27-associated spondyloarthropathy. Nineteen patients had one or more autoantibodies: ANA greater than or equal to 1:80 (n = 10); RF greater than or equal to 1:80 (n = 6); and positive lupus anticoagulant (n = 7). The seroreactivity of 10 of these patients remained unexplained. CONCLUSIONS: This neurologic population demonstrated significant seroreactivity and rheumatic disease associations, with SS and lupus anticoagulant-related neurologic disease the most common. Since SS and the antiphospholipid syndrome can be overlooked, it is recommended that a formal evaluation for SS and a direct lupus anticoagulant assay should be considered in the examination of patients with **neuropsychiatric symptoms** .

Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: *Antibodies, Antinuclear--analysis--AN; *Blood Coagulation Factors--immunology--IM; *Rheumatic Diseases--immunology--IM; *Rheumatoid Factor--analysis--AN; Adult; Aged; Aged, 80 and over; Antibodies, Antinuclear--immunology--IM; Blood Coagulation Factors--analysis--AN; Lupus Coagulation Inhibitor; Middle Aged; Prospective Studies; Questionnaires; Rheumatic Diseases--blood--BL; Rheumatic Diseases--diagnosis--DI; Sjogren's Syndrome--blood--BL; Sjogren's Syndrome--diagnosis--DI; Sjogren's Syndrome--immunology--IM
CAS Registry No.: 0 (Antibodies, Antinuclear); 0 (Blood Coagulation Factors); 0 (Lupus Coagulation Inhibitor); 9009-79-4 (Rheumatoid Factor)
Record Date Created: 19910509

Record Date Completed: 19910509

10/9/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08519880 PMID: 2335479

A prospective study of chronic or recurrent headache in systemic lupus erythematosus.

Vazquez-Cruz J; Traboulssi H; Rodriquez-De la Serna A; Geli C; Roig C; Diaz C

Department of Neurology, Sant Pau Hospital, Universitat Autonoma de Barcelona School of Medicine, Spain.

Headache (UNITED STATES) Mar 1990, 30 (4) p232-5, ISSN 0017-8748 Journal Code: 2985091R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

This study was conducted to analyze the prevalence and features of chronic or recurrent headache in Systemic Lupus Erythematosus (SLE), and also the relationship of such headache with other manifestations of the disease. A total of 76 patients (69 women and 7 men) with a mean age of 40 years (r: 24-74 years) were included. An overall severity index for SLE was applied. Fifty-two patients (68%) presented headache, 27 (52%) being vascular and 25 (48%) muscle contraction type. Headache in general was more frequent after the onset of SLE (p less than .001). Prevalence of muscle contraction headache in particular was greater following manifestations of SLE. Family history of **migraine** was recorded in 54% of the patients with vascular headache. This antecedent was more common in patients in whom **migraine** started before the onset of SLE (p = .05). A greater number of **neuropsychiatric symptoms** was observed in the patients with vascular headache and family history (p less than .02). Patients with thrombocytopenia presented headache less frequently (p less than .05). Our results showed headache, of both vascular and muscle contraction types, to be frequent in SLE. We note that there is an increased frequency of muscle contraction headache after the onset of SLE, and that there is a **migraine** -like headache directly related to SLE. Migrainous patients with familial history have a greater probability to suffer neuropsychiatric manifestations. Finally, it is suggested that severity of SLE is not related to presence of headache.

Tags: Female; Human; Male

Descriptors: *Headache--complications--CO; *Lupus Erythematosus, Systemic --complications--CO; Adult; Aged; Chronic Disease; Headache--epidemiology --EP; Infant, Newborn; Middle Aged; Prevalence; Prospective Studies; Recurrence

Record Date Created: 19900614
Record Date Completed: 19900614

?logoff hold

7015127 PMID: 15163088

Neuropsychiatric problems in tuberous sclerosis complex.

Asato Miya R; Hardan Antonio Y

Laboratory of Neurocognitive Development, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center, Pittsburgh, PA 15213, USA. asatomr@upmc.edu

Journal of child neurology (Canada) Apr 2004, 19 (4) p241-9, ISSN 0883-0738 Journal Code: 8606714

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Tuberous sclerosis complex is an autosomal dominant disorder characterized by abnormal cellular differentiation and proliferation, as well as abnormal neuronal migration. It is a disease affecting multiple organ systems and typically has brain involvement, causing severe disabilities. This article **reviews** the literature of the commonly associated **neuropsychiatric** complications, including mental retardation, autism-like features, and other **behavior** problems, which are discussed in the context of the neuropathology and **epilepsy** observed in tuberous sclerosis complex. The potential pathogenesis of neuropsychiatric problems is explored, including links to the genetics, neuropathology, neurotrophins, and **epilepsy** factors associated with tuberous sclerosis complex. Treatment of **neuropsychiatric symptoms** , including autism-like features, attention deficits, and sleep disorders, is also discussed. (83 Refs.)

includes donepezil, galanthamine and rivastigmine. Tacrine, the first acetylcholinesterase inhibitor who became available in 1993 as a treatment for AD, does not play an essential role anymore besides his historical value, because of its hepatotoxicity. Although acetylcholinesterase inhibitors are no cure, these drugs can delay the progress of mental deterioration, reduce **neuropsychiatric symptoms** and therefore represent a rational therapeutic approach to the treatment of Alzheimer's Disease. (134 Refs.)

Tags: Human

Descriptors: *Alzheimer Disease--drug therapy--DT; *Cholinesterase Inhibitors--therapeutic use--TU; Alzheimer Disease--metabolism--ME; Carbamates--adverse effects--AE; Carbamates--pharmacology--PD; Carbamates --therapeutic use--TU; Cholinesterase Inhibitors--adverse effects--AE; Cholinesterase Inhibitors--pharmacology--PD; Clinical Trials; Galantamine --adverse effects--AE; Galantamine--pharmacology--PD; Galantamine --therapeutic use--TU; Indans--adverse effects--AE; Indans--pharmacology --PD; Indans--therapeutic use--TU; Piperidines--adverse effects--AE; Piperidines--pharmacology--PD; Piperidines--therapeutic use--TU; Tacrine --adverse effects--AE; Tacrine--pharmacology--PD; Tacrine--therapeutic use--TU

CAS Registry No.: 0 (Carbamates); 0 (Cholinesterase Inhibitors); 0 (Indans); 0 (Piperidines); 120011-70-3 (donepezil); 123441-03-2 (rivastigmine); 321-64-2 (Tacrine); 357-70-0 (Galantamine)

Record Date Created: 20040202

Record Date Completed: 20040416

4/9/26 (Item 26 from file: 155)

15957725 PMID: 12895683

Salvia for dementia therapy: review **of pharmacological activity and pilot tolerability clinical trial.**

Perry Nicolette S L; Bollen Chloe; Perry Elaine K; Ballard Clive

Department of Pharmacology and Toxicology, University of Otago, Dunedin, New Zealand.

Pharmacology, biochemistry, and behavior (United States) Jun 2003, 75 (3) p651-9, ISSN 0091-3057 Journal Code: 0367050

Document type: Clinical Trial; Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

S. lavandulaefolia Vahl. (Spanish sage) extracts and constituents have demonstrated anticholinesterase, antioxidant, anti-inflammatory, oestrogenic and CNS depressant (sedative) effects all of which are currently relevant to the treatment of Alzheimer's disease (AD). The essential oil inhibits the enzyme acetylcholinesterase (AChE) from human brain tissue and bovine erythrocyte and individual monoterpenoid constituents inhibit AChE with varying degrees of potency. In vivo AChE inhibition of select brain (striatal and hippocampal over cortical) AChE was obtained following oral administration of the essential oil to rats. In a study in healthy volunteers essential oil administration produced significant effects on cognition. In a pilot open-label study involving oral administration of the essential oil to patients with AD, a significant increase in diastolic and systolic blood pressure was observed in two patients, however this may have been due primarily to preexisting hypertension and there were no abnormalities in other vital signs or blood samples during the trial period. Although an open label trial is not free from practice effects or rater-caregiver expectations, statistically significant differences between baseline and 6 weeks treatment were a reduction in **neuropsychiatric symptoms** and an improvement in attention. (70 Refs.)

Tags: Female; Human; Male

Descriptors: *Alzheimer Disease--drug therapy--DT; *Plants, Medicinal; *Salvia; Administration, Oral; Aged; Aged, 80 and over; Alzheimer Disease

--enzymology--EN; Animals; Cholinesterase Inhibitors--administration and dosage--AD; Cholinesterase Inhibitors--adverse effects--AE; Cholinesteras e Inhibitors--pharmacology--PD; Cholinesterase Inhibitors--therapeutic use --TU; Cholinesterases--blood--BL; Phytotherapy--methods--MT; Pilot Projects ; Plants, Medicinal--adverse effects--AE; Salvia--adverse effects--AE; Salvia--chemistry--CH
CAS Registry No.: 0 (Cholinesterase Inhibitors)
Enzyme No.: EC 3.1.1.8 (Cholinesterases)
Record Date Created: 20030804
Record Date Completed: 20040408

4/9/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15697877 PMID: 14502661
Use of functional imaging in Parkinsonism and dementia.
Burn David J; O'Brien John T
Department of Neurology, Regional Neurosciences Centre, Newcastle General Hospital, United Kingdom. d.j.burn@ncl.ac.uk
Movement disorders - official journal of the Movement Disorder Society (United States) Sep 2003, 18 Suppl 6 pS88-95, ISSN 0885-3185
Journal Code: 8610688
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Neuropsychiatric symptoms , including dementia, frequently coexist with parkinsonian disorders and may cause diagnostic confusion as well as management problems. Functional imaging studies include single photon emission computerised tomography (SPECT), positron emission tomography (PET), proton magnetic resonance spectroscopy, diffusion tensor imaging, and functional magnetic resonance imaging. This **review** addresses the utility of these techniques, from the clinician's perspective, focusing on the most common causes of parkinsonism and cognitive impairment, Parkinson's disease with dementia, dementia with Lewy bodies, and Alzheimer's disease. The potential and limitations of these techniques for accurate and early diagnosis, monitoring disease progression, and establishing the pathophysiological basis underlying key clinical features are considered. The development of new probes for SPECT and PET cameras capable of labeling protein aggregates (e.g., beta-amyloid) will offer exciting new insights into the spatial and temporal pattern of pathophysiological processes. Longitudinal studies with clinicopathological correlation represent the "gold standard" for fully evaluating functional imaging techniques. Copyright 2003 Movement Disorder Society (64 Refs.)
Tags: Comparative Study; Human
Descriptors: *Dementia--radionuclide imaging--RI; *Magnetic Resonance Imaging; *Magnetic Resonance Spectroscopy; *Neurodegenerative Diseases --diagnosis--DI; *Parkinson Disease--diagnosis--DI; *Tomography, Emission-Computed; *Tomography, Emission-Computed, Single-Photon; Brain --blood supply--BS; Brain--physiopathology--PP; Dementia--physiopathology --PP; Diagnosis, Differential; Energy Metabolism--physiology--PH; Neurodegenerative Diseases--physiopathology--PP; Parkinson Disease --physiopathology--PP; Predictive Value of Tests; Regional Blood Flow --physiology--PH
Record Date Created: 20030922
Record Date Completed: 20040224

4/9/33 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15675808 PMID: 14714910
The blood-brain barrier in systemic lupus erythematosus.

Abbott N J; Mendonca L L F; Dolman D E M
Centre for Neuroscience Research, King's College London, Guy's Campus, London SE1 1UL, UK. joan.abbott@kcl.ac.uk
Lupus (England) 2003, 12 (12) p908-15, ISSN 0961-2033
Journal Code: 9204265
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Central nervous system (CNS) involvement may occur in 20-70% of systemic lupus erythematosus (SLE) patients where neurological **symptoms** are overt; this is termed **neuropsychiatric** lupus or NPSLE. This **review** summarizes evidence that damage to the brain endothelium forming the blood-brain barrier (BBB) is a contributory factor in NPSLE. The normal CNS is protected by blood-tissue barriers at three sites, the brain endothelium (BBB), the choroid plexus epithelium (blood-CSF barrier) and the arachnoid epithelium. The tight junctions of the barrier layers severely restrict entry of plasma constituents including proteins, so that the CSF and brain interstitial fluid contain low levels of protein. Methods for diagnosing BBB damage include imaging (CT, MRI) using contrast agents, and analysing protein content and profiles of CSF Changes in the albumin quotient Qalbumin show evidence for barrier damage, while changes in the immunoglobulin (Ig) index can indicate intrathecal antibody production. However, BBB damage may be transient, and hence undetected or underestimated. Few mechanistic studies exist, but the two main candidate mechanisms for BBB damage are microthrombi in cerebral vessels leading to ischaemia, and immune-mediated attack and activation of the endothelium leading to local cytokine production. Both can result in barrier breakdown. Neurological syndromes could then be secondary to damage to the BBB. The implications for treatment of NPSLE are discussed. (80 Refs.)

Tags: Female; Human; Male
Descriptors: *Autoantibodies--immunology--IM; *Blood-Brain Barrier --immunology--IM; *Lupus Vasculitis, Central Nervous System--immunology--IM ; *Lupus Vasculitis, Central Nervous System--pathology--PA; Cerebrospinal Fluid Proteins--metabolism--ME; Endothelium, Vascular--physiology--PH; Lupus Erythematosus, Systemic--immunology--IM; Lupus Erythematosus, Systemic--pathology--PA; Prognosis; Risk Assessment
CAS Registry No.: 0 (Autoantibodies); 0 (Cerebrospinal Fluid Proteins)
Record Date Created: 20040112
Record Date Completed: 20040219

4/9/34 (Item 34 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15675806 PMID: 14714908
Quantitative magnetic resonance imaging in neuropsychiatric systemic lupus erythematosus.
Peterson P L; Howe F A; Clark C A; Axford J S
Lupus Research Unit, St Thomas' Hospital, London, UK. ppeterson@doctors.org.uk
Lupus (England) 2003, 12 (12) p897-902, ISSN 0961-2033
Journal Code: 9204265
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Neuropsychiatric symptoms are common in systemic lupus erythematosus (SLE) but are poorly understood. Although there is a wide spectrum of clinical manifestations, brain histology often simply shows a bland vasculopathy. Magnetic resonance techniques such as magnetic resonance spectroscopy, magnetization transfer imaging and diffusion weighted imaging have been used to try to improve our understanding of the pathophysiological mechanisms involved in neuropsychiatric lupus (NPSLE).

This article **reviews** the current literature on the use of these techniques and their possible future role as diagnostic tools in NPSLE. (46 Refs.)
Tags: Comparative Study; Female; Human; Male
Descriptors: *Brain--pathology--PA; *Image Processing, Computer-Assisted; *Lupus Vasculitis, Central Nervous System--diagnosis--DI; *Magnetic Resonance Imaging--methods--MT; Brain Mapping--methods--MT; Magnetic Resonance Spectroscopy--methods--MT; Sensitivity and Specificity
Record Date Created: 20040112
Record Date Completed: 20040219

4/9/46 (Item 46 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14012425 PMID: 9711366
Chronic fatigue syndrome: an immunological perspective.
Vollmer-Conna U; Lloyd A; Hickie I; Wakefield D
Inflammation Research Unit, School of Pathology, University of New South Wales, Sydney, Australia.
Australian and New Zealand journal of psychiatry (AUSTRALIA) Aug 1998, 32 (4) p523-7, ISSN 0004-8674 Journal Code: 0111052
Document type: Journal Article; Review; Review Literature
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
OBJECTIVE: The aim of this study is to **review** research examining an immunological basis for chronic fatigue syndrome (CFS) and to discuss how a disturbance in immunity could produce central nervous system (CNS)-mediated **symptoms** . METHOD: Data relevant to the hypothesis that abnormal cytokine release plays a role in the pathogenesis of CFS are **reviewed** as well as recent evidence relating to potential mechanisms by which immune products may enter the brain and produce a disturbance in CNS processes. RESULTS: Examinations of cytokine levels in patients with CFS have produced inconclusive results. Recent evidence suggests that abnormal release of cytokines within the CNS may cause neural dysfunction by a variety of complex mechanisms. CONCLUSION: **Neuropsychiatric symptoms** in patients with CFS may be more closely related to disordered cytokine production by glial cells within the CNS than to circulating cytokines. This possibility is discussed in the context of unresolved issues in the pathogenesis of CFS. (42 Refs.)
Tags: Human
Descriptors: *Central Nervous System--immunology--IM; *Cytokines --cerebrospinal fluid--CF; *Fatigue Syndrome, Chronic--immunology--IM; Central Nervous System--physiopathology--PP; Fatigue Syndrome, Chronic --cerebrospinal fluid--CF; Fatigue Syndrome, Chronic--physiopathology--PP; Infection--complications--CO; Infection--immunology--IM; Neuroglia --metabolism--ME
CAS Registry No.: 0 (Cytokines)
Record Date Created: 19981123
Record Date Completed: 19981123

4/9/47 (Item 47 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13996152 PMID: 9695456
Neuropsychiatric manifestations of Lyme disease.
Paparone P W
Lyme Disease Center for South Jersey, Absecon, NJ 08201, USA.
Journal of the American Osteopathic Association (UNITED STATES) Jul 1998, 98 (7) p373-8, ISSN 0098-6151 Journal Code: 7503065
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Lyme disease is a multisystem illness that may affect the central nervous system and subsequently produce mild to severe psychiatric disorders. Physicians who treat patient with Lyme disease need to be aware of its **neuropsychiatric symptoms**, which may emerge months to years after the initial infection. Prompt diagnosis and effective treatment are needed to avoid the debilitating and possibly irreversible mental illness associated with the neurologic involvement of this spirochetal infection. The author **reviews** the neuropsychiatric manifestations of Lyme disease and provides diagnostic and therapeutic approaches for the management of the central nervous system disease that may cause them. (19 Refs.)

Tags: Human

Descriptors: *Central Nervous System Diseases--microbiology--MI; *Lyme Disease--psychology--PX; *Psychotic Disorders--microbiology--MI

Record Date Created: 19980827
Record Date Completed: 19980827

4/9/48 (Item 48 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13933138 PMID: 9633685

Managing the neuropsychiatric symptoms **of Parkinson's disease.**

Lieberman A

Muhammad Ali Parkinson Research Center at Barrow Neurological Institute, Phoenix, AZ 85103, USA.

Neurology (UNITED STATES) Jun 1998, 50 (6 Suppl 6) pS33-8; discussion S44-8, ISSN 0028-3878 Journal Code: 0401060

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Neuropsychiatric symptoms frequently complicate the treatment of Parkinson's disease (PD). Approximately 27% of PD patients are demented, and approximately 19% are cognitively impaired without being demented. These 46% of patients are prone to development of delirium when they take antiparkinsonian drugs. Approximately 40% of PD patients are depressed. The depression may be endogenous or exogenous, apathetic or agitated. Approximately 40% of PD patients are anxious or have panic attacks. The attacks may or may not be associated with depression. This article **reviews** the diagnosis of these **symptoms** and discusses their management. (40 Refs.)

Tags: Human

Descriptors: *Antiparkinson Agents--administration and dosage--AD; *Dementia--drug therapy--DT; *Neuropsychological Tests; *Parkinson Disease --drug therapy--DT; *Psychotropic Drugs--administration and dosage--AD; Antiparkinson Agents--adverse effects--AE; Dementia--diagnosis--DI; Diagnosis, Differential; Drug Therapy, Combination; Parkinson Disease --diagnosis--DI; Prognosis; Psychotropic Drugs--adverse effects--AE

CAS Registry No.: 0 (Antiparkinson Agents); 0 (Psychotropic Drugs)

Record Date Created: 19980625
Record Date Completed: 19980625

?s s4 and (epilepsy? or parkinson? or fibromyal? or pain? or migrane? or headache? or alzheimer?)
Processed 20 of 26 files ...
Processing
Completed processing all files
1144 S4
358646 EPILEPSY?
258822 PARKINSON?
21666 FIBROMYAL?
1515300 PAIN?
1569 MIGRANE?

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          230411  HEADACHE?
          340166  ALZHEIMER?
      S5     456  S4 AND (EPILEPSY? OR PARKINSON? OR FIBROMYAL? OR PAIN? OR
                  MIGRANE? OR HEADACHE? OR ALZHEIMER?)
?ds

Set     Items   Description
S1       7104   NEUROPSYCHIAT? (10N) (SYMPTOM? OR BEHAVIOR? OR MOTOR? OR P-
            HYSICAL?)
S2    5930254   REVIEW? OR TUTOR?
S3       1457   S1 AND S2
S4       1144   S3 AND SYMPTOM?
S5        456   S4 AND (EPILEPSY? OR PARKINSON? OR FIBROMYAL? OR PAIN? OR -
            MIGRANE? OR HEADACHE? OR ALZHEIMER?)
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?t s5/6,kwic/1-25
>>>KWIC option is not available in file(s): 399
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5/6,KWIC/1 (Item 1 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

17804954 PMID: 15658502
[Neuropsychiatric disorders and GABA]
Oct 2004

... functions. Therefore, abnormalities in a GABAergic signaling molecule would lead to a crisis of severe **symptoms** relevant to a number of **neuropsychiatric** disorders. These include **epilepsy** , depression, schizophrenia, stiff-person syndrome, drug addiction and so on. In this **review** article, we will summarize recent studies on the relationship between the malfunction of GABAergic signaling...

5/6,KWIC/2 (Item 2 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

17671898 PMID: 15550268
Crimean-Congo hemorrhagic fever.
Dec 2004

... short incubation period, CCHF is characterized by a sudden onset of high fever, chills, severe **headache** , dizziness, back, and abdominal **pains** . Additional **symptoms** can include nausea, vomiting, diarrhea, **neuropsychiatric** , and cardiovascular changes. In severe cases, hemorrhagic manifestations, ranging from petechiae to large areas of...

...for contracting disease; however, other important risk factors are known and are discussed in this **review** . In recent years, major advances in the molecular detection of CCHFV, particularly the use of...

... knowledge of its basic biology, may lead to improved therapies in the future. This article **reviews** the history, epidemiology, ecology, clinical features, pathogenesis, diagnosis, and treatment of CCHF. In addition, recent...

5/6,KWIC/3 (Item 3 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

17579699 PMID: 15582913
Nicotinic receptor mechanisms and cognition in normal states and neuropsychiatric disorders.
Dec 2004

... Studies conducted in a variety of neuropsychiatric populations [e.g. attention-deficit hyperactivity disorder (ADHD), **Alzheimer** 's disease,

schizophrenia] have collectively suggested that nicotine may be efficacious in remediating selected cognitive...

... by nicotine administration in healthy subjects with normal cognitive function is less clear. This article **reviews** our current understanding of central nicotinic acetylcholine receptor (nAChRs) systems in normal and neuropsychiatric disease states and, specifically, their role with respect to cognitive dysfunction and clinical **symptoms** in several specific **neuropsychiatric** populations, including ADHD, **Alzheimer** 's disease, **Parkinson** 's disease, Tourette's Disorder, schizophrenia and affective disorders. The potential benefits of nicotinic agents...

5/6,KWIC/4 (Item 4 from file: 155)

17015127 PMID: 15163088
Neuropsychiatric problems in tuberous sclerosis complex.
Apr 2004

... disease affecting multiple organ systems and typically has brain involvement, causing severe disabilities. This article **reviews** the literature of the commonly associated **neuropsychiatric** complications, including mental retardation, autism-like features, and other **behavior** problems, which are discussed in the context of the neuropathology and **epilepsy** observed in tuberous sclerosis complex. The potential pathogenesis of neuropsychiatric problems is explored, including links to the genetics, neuropathology, neurotrophins, and **epilepsy** factors associated with tuberous sclerosis complex. Treatment of **neuropsychiatric symptoms** , including autism-like features, attention deficits, and sleep disorders, is also discussed.
; Autistic Disorder--complications--CO; Autistic Disorder--psychology --PX; Autistic Disorder--therapy--TH; Child; Child, Preschool; **Epilepsy** --complications--CO; **Epilepsy** --drug therapy--DT; **Epilepsy** --psychology --PX; Infant; Learning Disorders--complications--CO; Learning Disorders --psychology--PX; Mental Disorders--therapy--TH...

5/6,KWIC/5 (Item 5 from file: 155)

16895999 PMID: 15181787
[Typical benign epilepsy **potentials in childhood (Rolandic spikes)--neurobiological and neuropsychological** symptoms **and their clinical significance in child and adolescent psychiatry]**
Benigne epilepsietypische Potentiale des Kindesalters (Rolando-Spikes)--n eurobiologische und neuropsychologische Befunde und ihre klinische Bedeutung in der Kinder- und Jugendpsychiatrie.
May 2004

[Typical benign epilepsy **potentials in childhood (Rolandic spikes)--neurobiological and neuropsychological** symptoms **and their clinical significance in child and adolescent psychiatry]**
INTRODUCTION: Rolandic **epilepsy** is the most frequent epileptic syndrome in childhood, electroencephalographically characterized by focal sharp waves, so...

... 2.4% of children; only 10% of them suffer from epileptic seizures. METHODS: This paper **reviews** genetic, epidemiological, radiological, neurophysiologic, metabolic and neuropsychological findings in children with rolandic discharges. RESULTS: The...
... favorable, seizures and EEG features usually resolve completely at puberty. In contrast to former assumptions, **symptoms** range from infrequent seizures to neuropsychological deficits and behavior problems, even in children without overt...

... role of a hereditary impairment of brain maturation. CONCLUSIONS: The

benefit of pharmacotherapy for treating **neuropsychiatric symptoms** in children with rolandic spikes but without overt seizures remains to be clarified.

Descriptors: *Cerebral Cortex--physiopathology--PP; *Electroencephalography; * **Epilepsy** , Rolandic--genetics--GE; *Neuropsychological Tests...; Disorders--genetics--GE; Child Behavior Disorders--physiopathology--PP; Child Behavior Disorders--psychology--PX; Child, Preschool; **Epilepsy** , Rolandic--diagnosis--DI; **Epilepsy** , Rolandic--physiopathology--PP; **Epilepsy** , Rolandic--psychology--PX; Evoked Potentials--physiology--PH; Genetic Predisposition to Disease--genetics--GE; Infant; Language...

5/6,KWIC/6 (Item 6 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

16008085 PMID: 14754384
Acetylcholinesterase inhibition in Alzheimer **'s Disease.**
2004

Acetylcholinesterase inhibition in Alzheimer **'s Disease.**

Alzheimer 's Disease (AD) is the most common cause for dementia in our ageing population, which...

... to understand the neurobiology of cognition and to develop therapeutic tools for the fight against **Alzheimer** 's Disease. Acetylcholinesterase inhibitors are currently the best established treatment for this devastating disease. This **review** describes historical aspects and the vast range of use of cholinesterase inhibitors in traditional societies...

... hypotheses of AD. Third, acetylcholinesterase inhibitors currently available for the treatment of AD will be **reviewed** . This includes donepezil, galanthamine and rivastigmine. Tacrine, the first acetylcholinesterase inhibitor who became available in...

... acetylcholinesterase inhibitors are no cure, these drugs can delay the progress of mental deterioration, reduce **neuropsychiatric symptoms** and therefore represent a rational therapeutic approach to the treatment of **Alzheimer** 's Disease.

Descriptors: ***Alzheime** r Disease--drug therapy--DT; *Cholinesterase Inhibitors--therapeutic use--TU; **Alzheimer** Disease--metabolism--ME; Carbamates--adverse effects--AE; Carbamates--pharmacology--PD; Carbamates --therapeutic use--TU; Cholinesterase...

5/6,KWIC/7 (Item 7 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

15957725 PMID: 12895683
Salvia for dementia therapy: review **of pharmacological activity and pilot tolerability clinical trial.**
Jun 2003

Salvia for dementia therapy: review **of pharmacological activity and pilot tolerability clinical trial.**

... and CNS depressant (sedative) effects all of which are currently relevant to the treatment of **Alzheimer** 's disease (AD). The essential oil inhibits the enzyme acetylcholinesterase (AChE) from human brain tissue...

... caregiver expectations, statistically significant differences between baseline and 6 weeks treatment were a reduction in **neuropsychiatric symptoms** and an improvement in attention.

Descriptors: ***Alzheime** r Disease--drug therapy--DT; *Plants, Medicinal; *Salvia; Administration, Oral; Aged; Aged, 80 and over; **Alzheimer** Disease --enzymology--EN; Animals; Cholinesterase Inhibitors--administration and dosage--AD; Cholinesterase Inhibitors--adverse effects--AE...

5/6,KWIC/8 (Item 8 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

15726765 PMID: 14564129
Cholinesterase inhibitor therapies and neuropsychiatric manifestations of Alzheimer **'s disease.**
2004

Cholinesterase inhibitor therapies and neuropsychiatric manifestations of Alzheimer **'s disease.**
BACKGROUND: **Neuropsychiatric symptoms** (NPS) of **Alzheimer** 's disease (AD) occur throughout the course of AD. Behaviors include mood alterations, psychosis, agitation, and apathy. These **symptoms** are a major cause of diminished quality of life for both patients and caregivers. Evidence...

... the receptors. This effect is believed to be beneficial in improving or stabilizing many behavioral **symptoms** of AD. Preliminary studies of ChE-Is have shown mixed results; however, the results of more recent studies have been favorable. OBJECTIVES: To **review** major trials of ChE-Is and summarize effects on behavioral **symptoms** . Agents **reviewed** include donepezil, galantamine, rivastigmine, tacrine, and metrifonate. RESULTS: The **review** of the studies favors a benefit of the ChE-Is in reducing NPS. Of the...
...the treatment group even if statistical significance was not reached. In some studies, specific behavioral **symptoms** , particularly apathy and hallucinations, were reduced. CONCLUSIONS: Evidence suggests that ChE-Is have psychotropic effects and may be of value in managing **neuropsychiatric behavioral symptoms** in AD. Further studies will be necessary to fully understand the potential of these agents...
Descriptors: ***Alzheime*** r Disease--drug therapy--DT; * **Alzheimer** Disease--psychology--PX; *Cholinesterase Inhibitors--therapeutic use--TU

5/6,KWIC/9 (Item 9 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

15726764 PMID: 14564128
Treating apathy in Alzheimer **'s disease.**
2004

Treating apathy in Alzheimer **'s disease.**
Apathy, a syndrome of decreased initiation and motivation, affects over 70% of individuals with **Alzheimer** 's disease (AD) and is the most common **neuropsychiatric symptom** reported in AD patients. The syndrome of apathy is associated with functional impairment among patients...

... reflect the interaction between cholinergic deficiency and neuropathological changes in frontal brain regions. This article **reviews** the assessment and treatment of apathy in AD, with emphasis on the utility of acetylcholinesterase...
Descriptors: ***Alzheime*** r Disease--psychology--PX; *Cholinesterase Inhibitors--therapeutic use--TU; *Mood Disorders--drug therapy--DT; *Motivation; Aged; **Alzheimer** Disease--complications--CO; Mood Disorders --etiology--ET; Social Behavior

5/6,KWIC/10 (Item 10 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

15697877 PMID: 14502661
Use of functional imaging in Parkinsonism **and dementia.**
Sep 2003

Use of functional imaging in Parkinsonism **and dementia.**
Neuropsychiatric symptoms , including dementia, frequently coexist with **parkinsonian** disorders and may cause diagnostic confusion as well as management problems. Functional imaging studies include...

... tomography (PET), proton magnetic resonance spectroscopy, diffusion tensor imaging, and functional magnetic resonance imaging. This **review** addresses the utility of these techniques, from the clinician's perspective, focusing on the most common causes of **parkinsonism** and cognitive impairment, **Parkinson** 's disease with dementia, dementia with Lewy bodies, and **Alzheimer** 's disease. The potential and limitations of these techniques for accurate and early diagnosis, monitoring...

Descriptors: *Dementia--radionuclide imaging--RI; *Magnetic Resonance Imaging; *Magnetic Resonance Spectroscopy; *Neurodegenerative Diseases --diagnosis--DI; * **Parkinson** Disease--diagnosis--DI; *Tomography, Emission-Computed; *Tomography, Emission-Computed, Single-Photon...; physiopathology--PP; Dementia--physiopathology--PP; Diagnosis, Differential ; Energy Metabolism--physiology--PH; Neurodegenerative Diseases --physiopathology--PP; **Parkinson** Disease--physiopathology--PP; Predictive Value of Tests; Regional Blood Flow--physiology--PH

5/6,KWIC/11 (Item 11 from file: 155)

15572400 PMID: 14594099

Dementia with Lewy bodies. Review **of diagnosis and pharmacologic management.**
Oct 2003

Dementia with Lewy bodies. Review **of diagnosis and pharmacologic management.**

OBJECTIVE: To **review** clinical features of dementia with Lewy bodies (DLB) and to guide family physicians in pharmacologic...

... was available for diagnosis and treatment of DLB. One randomized controlled trial of rivastigmine was **reviewed** and appraised. MAIN MESSAGE: Dementia with Lewy bodies is common. Diagnosis can be made by...

... criteria including presence of dementia with marked fluctuation in performance, hallucinations, and the onset of **parkinsonism** . Cholinesterase inhibitors should be considered for **neuropsychiatric symptoms** . Levodopa-carbidopa combinations should be considered for treatment of **parkinsonism** . Neuroleptics should be used with caution because of the risk of serious sensitivity reactions. If...

5/6,KWIC/12 (Item 12 from file: 155)

15495356 PMID: 14693108

Dementia with Lewy bodies.
Jan 2004

... of the clinical and pathological characteristics of the dementia that occurs during the course of **Parkinson** 's disease. Here we **review** the current state of scientific knowledge on DLB. Accurate identification of patients is important because they have specific **symptoms** , impairments, and functional disabilities that differ from those of other common types of dementia. Severe...

... Treatment with cholinesterase inhibitors is well tolerated by most patients and substantially improves cognitive and **neuropsychiatric symptoms** . Clear guidance on the management of DLB is urgently needed. Virtually unrecognised 20 years ago...

; **Alzheimer** Disease--pathology--PA; **Alzheimer** Disease --physiopathology--PP; Brain--radiography--RA; Clinical Trials; Diagnosis, Differential; Lewy Body Disease--diagnosis--DI...

...pathology--PA; Lewy Body Disease--physiopathology--PP; Lewy Body Disease--therapy--TH; Magnetic Resonance Imaging; **Parkinson** Disease

--pathology--PA; **Parkinson** Disease--physiopathology--PP; Tomography, Emission-Computed, Single-Photon; Treatment Outcome

5/6,KWIC/13 (Item 13 from file: 155)
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14041785 PMID: 9741073
The uses of psychotropics in symptom **management in advanced cancer.**
Jul-Aug 1998

The uses of psychotropics in symptom **management in advanced cancer.**
...of progressive disease. Psychotropic drugs are frequently used for the management of physical and psychosocial **symptoms** in these patients. Thalidomide, cannabinoids and melatonin are emerging agents for the management of cachexia...

... anti-depressants and newer anti-depressants also have an established role in the management of **neuropsychiatric symptoms** such as delirium or depression. Cancer patients present unique challenges for successful psychotropic therapy including...

... borderline cognition, opioid and psychotropic therapy. A practical clinical approach which defines a specific target **symptom** , an outcome latency period, expected side effects, and **reviews** possible drug interactions, and frequent monitoring is outlined. Continued research is needed to further define the role of psychotropics in the management of the different physical and psychosocial **symptoms** in advanced cancer patients.
; Cachexia--drug therapy--DT; Disease Progression; Neoplasms --complications--CO; **Pain** --drug therapy--DT; Palliative Care

5/6,KWIC/14 (Item 14 from file: 155)
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13933138 PMID: 9633685
Managing the neuropsychiatric symptoms **of** Parkinson **'s disease.**
Jun 1998

Managing the neuropsychiatric symptoms **of** Parkinson **'s disease.**
Neuropsychiatric symptoms frequently complicate the treatment of **Parkinson** 's disease (PD). Approximately 27% of PD patients are demented, and approximately 19% are cognitively...

... have panic attacks. The attacks may or may not be associated with depression. This article **reviews** the diagnosis of these **symptoms** and discusses their management.
Descriptors: *Antiparkinson Agents--administration and dosage--AD; *Dementia--drug therapy--DT; *Neuropsychological Tests; * **Parkinson** Disease--drug therapy--DT; *Psychotropic Drugs--administration and dosage --AD; Antiparkinson Agents--adverse effects--AE; Dementia--diagnosis--DI; Diagnosis, Differential; Drug Therapy, Combination; **Parkinson** Disease --diagnosis--DI; Prognosis; Psychotropic Drugs--adverse effects--AE

5/6,KWIC/15 (Item 15 from file: 155)
DIALOG(R)File 155:(c) format only 2005 The Dialog Corp. All rts. reserv.

13332277 PMID: 9003973
Posterior fossa lesions associated with neuropsychiatric symptomatology .
Nov 1996

Posterior fossa lesions associated with neuropsychiatric symptomatology .
We **reviewed** 7 cases with posterior fossa structural abnormalities (3 tumors, 2 megacisterna magna and 2 Dandy-Walker syndrome) presenting with

neuropsychiatric symptomatology . Derangement in the balance of dopamine, serotonin and noradrenergic networks has been implicated in the ...

...Descriptors: Cranial Fossa, Posterior; *Dandy-Walker Syndrome --psychology--PX; *Delirium, Dementia, Amnestic, Cognitive Disorders --etiology--ET; * **Epilepsy** , Complex Partial--etiology--ET; *Glioma --psychology--PX; *Mental Disorders--etiology--ET; *Neuroblastoma --psychology--PX; *Pons...

5/6,KWIC/16 (Item 16 from file: 155)

13051502 PMID: 8732586
Schizophrenia and Alzheimer **'s disease: clinical and pathophysiologic analogies.**
May-Jun 1996

Schizophrenia and Alzheimer **'s disease: clinical and pathophysiologic analogies.**

Psychotic **symptoms** are prominent in schizophrenia and a frequent **neuropsychiatric** manifestation of **Alzheimer** 's disease (AD), occurring in approximately 50% of patients affected. The shared psychiatric **symptoms** suggest common cerebral pathophysiologies. Radiologic and pathologic findings indicate a predilection toward limbic involvement, with...

... different, but they have similarities in the pattern of regional brain dysfunction, biochemical dysfunction, and **symptomatology** . We represent a selective **review** of these similarities. Insights drawn from these observations enrich the understanding of each disorder.

Descriptors: ***Alzheime** r Disease--diagnosis--DI; *Schizophrenia --diagnosis--DI; Acetylcholine--physiology--PH; Adult; Aged; **Alzheimer** Disease--pathology--PA; **Alzheimer** Disease--psychology--PX; Atrophy; Diagnostic Imaging; Dopamine--physiology--PH; Limbic System--pathology--PA; Middle Aged...

5/6,KWIC/17 (Item 17 from file: 155)

12901374 PMID: 8554655
Neurologic manifestations of pediatric systemic lupus erythematosus.
Oct 1995

Central nervous system involvement is a common but rarely **reviewed** feature of pediatric systemic lupus erythematosus (SLE). We retrospectively **reviewed** the charts of 91 patients with pediatric SLE and using a standardized data abstraction form...

... of SLE was 13.3 years. In 19 patients the CNS manifestation was a presenting **symptom** , in 12 patients CNS involvement was present within the first year of diagnosis, and in...

... papilledema (5%), and 2 patients had a peripheral neuropathy (5%). Nine patients (22%) had severe **headache** consistent with lupus **headache** . Seven children had more than one CNS manifestation. In the investigation of CNS-SLE, computed...

... only in 33% of patients with seizure disorders and rarely helpful in patients with diffuse **neuropsychiatric symptoms** . Single-photon emission computed tomography scans were abnormal in most patients with neuropsychiatric SLE, especially...

5/6,KWIC/18 (Item 18 from file: 155)

12477471 PMID: 12917981
Cholinesterase inhibitors for dementia with Lewy bodies.
2003

...cases of dementia among people aged over 65, although autopsy suggests much lower rates. Characteristic **symptoms** are dementia, marked fluctuation of cognitive ability, early and persistent visual hallucinations and spontaneous motor features of **Parkinsonism** . Falls, syncope, transient disturbances of consciousness, neuroleptic sensitivity, and hallucinations in other modalities are also common. This combination of features can be difficult to manage as neuroleptics can make the **Parkinsonian** and cognitive **symptoms** worse. There is evidence to suggest that the cholinesterase inhibitors may be beneficial in this...

... case series indicate that cholinesterase inhibitors are safe, and will improve both cognitive deficits and **neuropsychiatric symptoms** in DLB. OBJECTIVES: To assess the use of cholinesterase inhibitors in DLB. SEARCH STRATEGY: The...

... compared with alternative interventions in patients with DLB are included. DATA COLLECTION AND ANALYSIS: Two **reviewers** (TP, RW) independently assessed quality of trials according to criteria described in the Cochrane Collaboration...

... Six months and longer).The primary outcome measures of interest are in the following areas: **neuropsychiatric** features. i.e. psychiatric **symptoms** and behavioural disturbances, cognitive function, activities of daily living, global assessments, quality of life, including...

... these results showed no difference between the two groups at 20 weeks using ITT analysis. **REVIEWER** 'S CONCLUSIONS: Patients with dementia with Lewy bodies who suffer from behavioural disturbance oS CONCLUSIONS...

5/6,KWIC/19 (Item 19 from file: 155)

12409012 PMID: 12804486
Anticholinergics for symptomatic **management of** Parkinson **'s disease.**
2003

Anticholinergics for symptomatic **management of** Parkinson **'s disease.**
BACKGROUND: Anticholinergics were the first drugs available for the **symptomatic** treatment of **Parkinson** 's disease and they are still widely used today, both as monotherapy and as part...

... events. They have been claimed to exert a better effect on tremor than on other **parkinsonian** features. OBJECTIVES: To determine the efficacy and tolerability of anticholinergics in the **symptomatic** treatment of **Parkinson** 's disease compared to placebo or no treatment. SEARCH STRATEGY: The literature search included electronic...

... as well as handsearching the neurology literature including the reference lists of identified articles, other **reviews** and book chapters. SELECTION CRITERIA: Randomised controlled trials of anticholinergic drugs versus placebo or no treatment in de-novo or advanced **Parkinson** 's disease, either as monotherapy or as an add-on to other antiparkinsonian drugs were...
... well as incomplete reporting precluded combined statistical analysis. Five studies used both tremor and other **parkinsonian** features as outcome measures. Outcome measures in these five studies were too different for a ...

...from studies was in patients on placebo due to withdrawal from pre-trial anticholinergic treatment. **REVIEWER** 'S CONCLUSIONS: As monotherapy or as an adjunct to other antiparkinsonian drugs, anticholinergics are more effective than placebo in improving **motor** function in **Parkinson** 's

- **Lateral,** away from the midline.
- **Medial,** toward the midline.
- **Posterior,** back side of the body, also known as the **dorsal**.
- **Proximal,** closest part nearest the trunk or head.
- **Superior,** above or near the head, also known as **cranial**.
- **Supra-,** prefix meaning above or over.
- **Ventral,** front side of the body, also known as **anterior**.

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Parts of the Human Skull

- **Calvarium,** includes the brain case.
- **Cranium,** includes the face and the calvarium.
- **Mandible,** the lower jaw.
- **Skull,** includes both the cranium and mandible.

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Bones of the Skull

- **Ethmoid bone,** sieve-like spongy bone located in the anterior part of the floor of the cranium between the orbits. The ethmoid is the principal supporting structure of the nasal cavity.
- **Frontal bone,** forms the forehead, the roofs of the orbits, and most of the anterior part of the cranial floor.
- **Inferior Nasal Conchae,** one of three scroll-like bones that project from the lateral wall of the nasal cavity. The inferior nasal conchae articulate with the ethmoid, maxilla, lacrimal and paltine bones and form the lower part of the lateral wall of the nasal cavity.
- **Lacrimal bone,** a thin scalelike bone, roughly resembling a fingernail in size and shape, at the anterior part of the medial wall of the orbit, articulating with the frontal and ethmoidal bones and the maxilla and inferior nasal concha.
- **Mandible,** the bone forming the lower jaw; the largest and strongest bone of the face, presenting a body and a pair of rami, which articulate with the skull at the tempromandibular joints.
- **Maxillae,** paired bones uniting to form the upper jawbone. The maxillae articulate with every bone of the face except the mandible, or lower jawbone.

cranium , pl. **crania** (krā′nē-ŭm, -ă) [TA]

The bones of the head collectively. In a more limited sense, the neurocranium, the bony brain case containing the brain, excluding the bones of the face (viscerocranium). Syn: skull

[Mediev. L. fr. G. *kranion*]

Prev

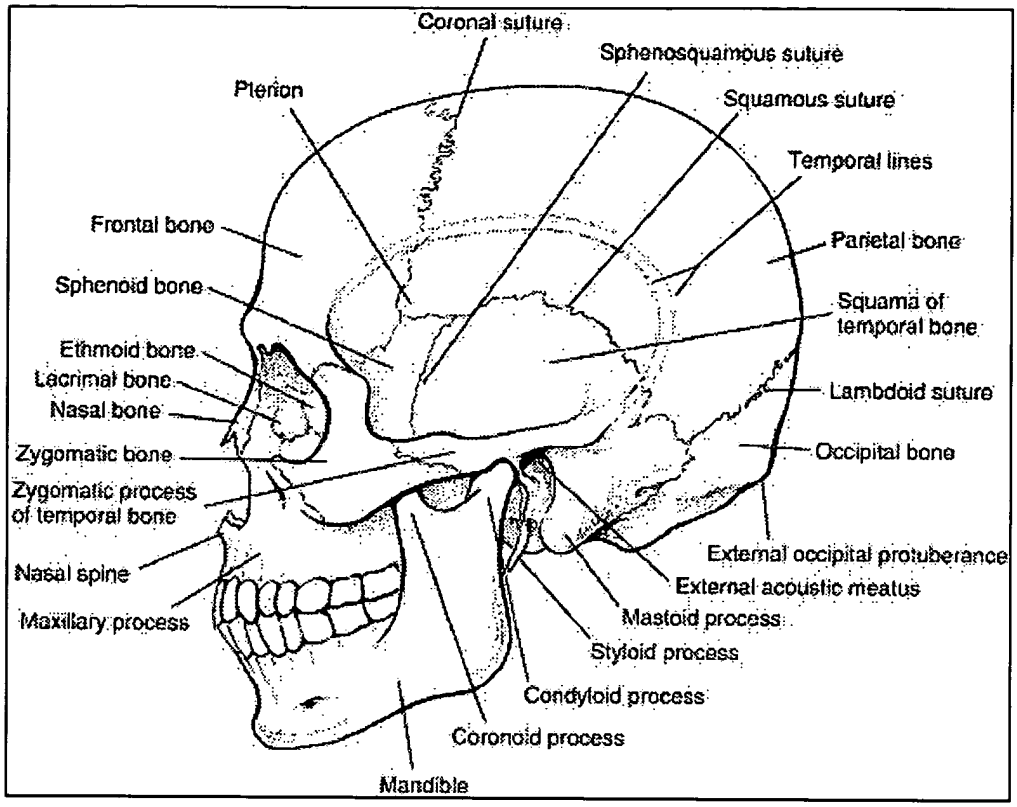
skull

A school, company, or shoal. "A knavish skull of boys and girls did pelt at him." "These fishes enter in great flotes and skulls." (Holland)

See: School a multitude.

1. <anatomy> The skeleton of the head of a vertebrate animal, including the brain case, or cranium, and the bones and cartilages of the face and mouth.

skull (skull) (skul) the skeleton of the head, including the cranium and the mandible. See illustration.



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Glossary of Skeletal Anatomy

Planes of the Body

Direction and Location

Parts of the Human Skull

Bones of the Skull

Bone Morphology

Planes of the Body

- **Coronal Plane,** divides the body into front and rear sections. Also called the **frontal plane**.
- **Frontal plane,** divides the body into front and rear sections. Also called the **coronal plane**.
- **Horizontal Plane,** divides the body into a superior (or upper) and an inferior (or lower) section. Also called the **transverse plane**.
- **Median Plane,** divides the body into right and left halves. Also called the **midsagittal plane**.
- **Midsagittal Plane,** divides the body into right and left halves. Also called the **median plane**.
- **Transverse Plane,** divides the body into a superior (or upper) and an inferior (or lower) section. Also called the **horizontal plane**.

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Direction and Location

- **Anterior,** front side of the body, also known as **ventral**.
- **Caudal,** in quadrapeds, the tail end [see **inferior**].
- **Cranial,** above or near the head, also known as **superior**.
- **Distal,** farthest end from the trunk or head.
- **Dorsal,** back side of the body, also known as the **posterior**.
- **Inferior,** below also, toward the feet.
- **Infra-,** prefix meaning below or under.

- **Nasal bone,** small oblong bones that meet at the middle and superior part of the face. Their fusion forms the superior part of the bridge of the nose.
- **Occipital bone,** a single trapezoid-shaped bone situated at the posterior and inferior part of the cranium.
- **Palatine bone,** one of two irregularly shaped bones (L-shaped) forming the posterior part of the hard palate, the lateral wall of the nasal fossa between the medial pterygoid plate and the maxilla, and the posterior part of the floor of the orbit. The posterior part of the hard palate, which separates the nasal cavity from the oral cavity, is formed by the horizontal plates.
- **Vomer,** a roughly triangular bone that forms the inferior and posterior of the nasal septum.
- **Parietal bones,** one of the two quadrilateral bones bones on either side of the cranium forming part of the superior and lateral surfaces of the skull, and joining each other in the midline at the sagittal suture. The parietal bones form the greater portion of the sides and roof of the cranial cavity.
- **Sphenoid bone,** a single, irregular, wedge-shaped bone at the base of the skull, which forms a part of the floor of the anterior, middle, and posterior cranial fossae. This bone is referred to as the keystone of the cranial floor because it articulates with all the other cranial bones.
- **Temporal bone,** one of the two irregular bones on either side of the skull forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. The temporal bones form the inferior sides of the cranium and part of the cranial floor.
- **Zygomatic bone,** the triangular bones on either side of the face below the eyes, commonly referred to as the cheekbones, they form the prominences of the cheeks and part of the outer wall and floor of the orbits.

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Bone Morphology

- **Crest,** a narrow prominent ridge.
- **Condyle,** a smooth rounded projection for articulation with another bone.
- **Epiphysis,** the end of a long bone that is originally separated from the main bone by a layer of cartilage but that later becomes united to the main

bone through ossification [compare to **suture** and **symphysis**].

- **Foramen,** a true hole in the bone [e.g. foramen magnum, incisive foramen.
- **Line,** a narrow raised ridge.
- **Meatus,** a small tubular opening.
- **Sulcus,** a groove.
- **Suture,** the line formed by the junction of two bones or an immovable joint between two bones, especially of the skull [compare to **epiphysis** and **symphysis**].
- **Symphysis,** the line or junction formed by a cartilaginous articulation between two bones without an intervening synovial membrane, this articulation often fuses as in the two bones and the two halves of the mandibles [compare to **suture** and **epiphysis**].
- **Trochanter,** a large rounded projection for muscle attachment.

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Last update: 19 May 2003

Related Kelly Webworks: **Med Anth** | **Prehistory** | **Melanesia** | **Forensic Crime Lab** | **IGHC** | **Plagiocephaly**

BioAnth Home

¤

pons (pons) (ponz) gen. *pon'tis* pl. *pon'tes* [L. "bridge"] [TA] 1. bridge: any slip of tissue connecting two parts of an organ. 2. the part of the central nervous system lying between the medulla oblongata and the mesencephalon, superior to the cerebellum; it consists of an anterior and a posterior part (see *pars basilaris pontis* and *tegmentum pontis*). Called also *p. cerebelli*. See Plate 11. See also *brainstem*.

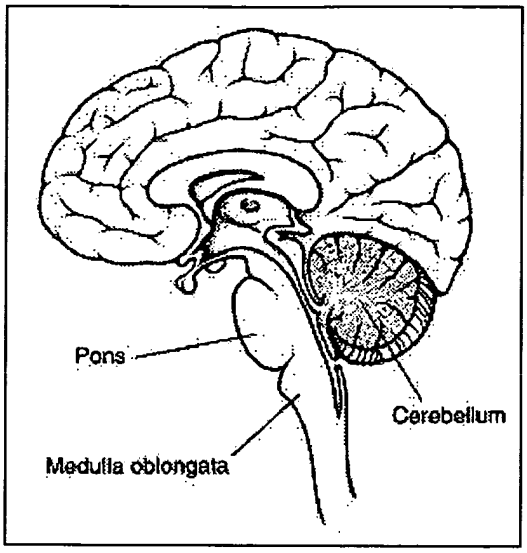

Figure P-54

pons cerebel'li, pons (def. 2).

pons et cerebel'lum, TA alternative for *metencephalon* (def. 1).

pons he'patis, an occasional projection of fibers partially bridging the longitudinal fissure of the liver.

brain (brain) (br[amacr]n) [Anglo-Saxon *braegen*] that part of the central nervous system contained within the cranium, comprising the prosencephalon (forebrain: telencephalon plus diencephalon), mesencephalon (midbrain), and rhombencephalon (hindbrain: metencephalon plus myelencephalon). It is derived (developed) from the anterior part of the embryonic neural tube. Functions include muscle control and coordination, sensory reception and integration, speech production, memory storage, and the elaboration of thought and emotion. See also *cerebrum*. Called also *encephalon* [TA].See Plates 11 and 12.

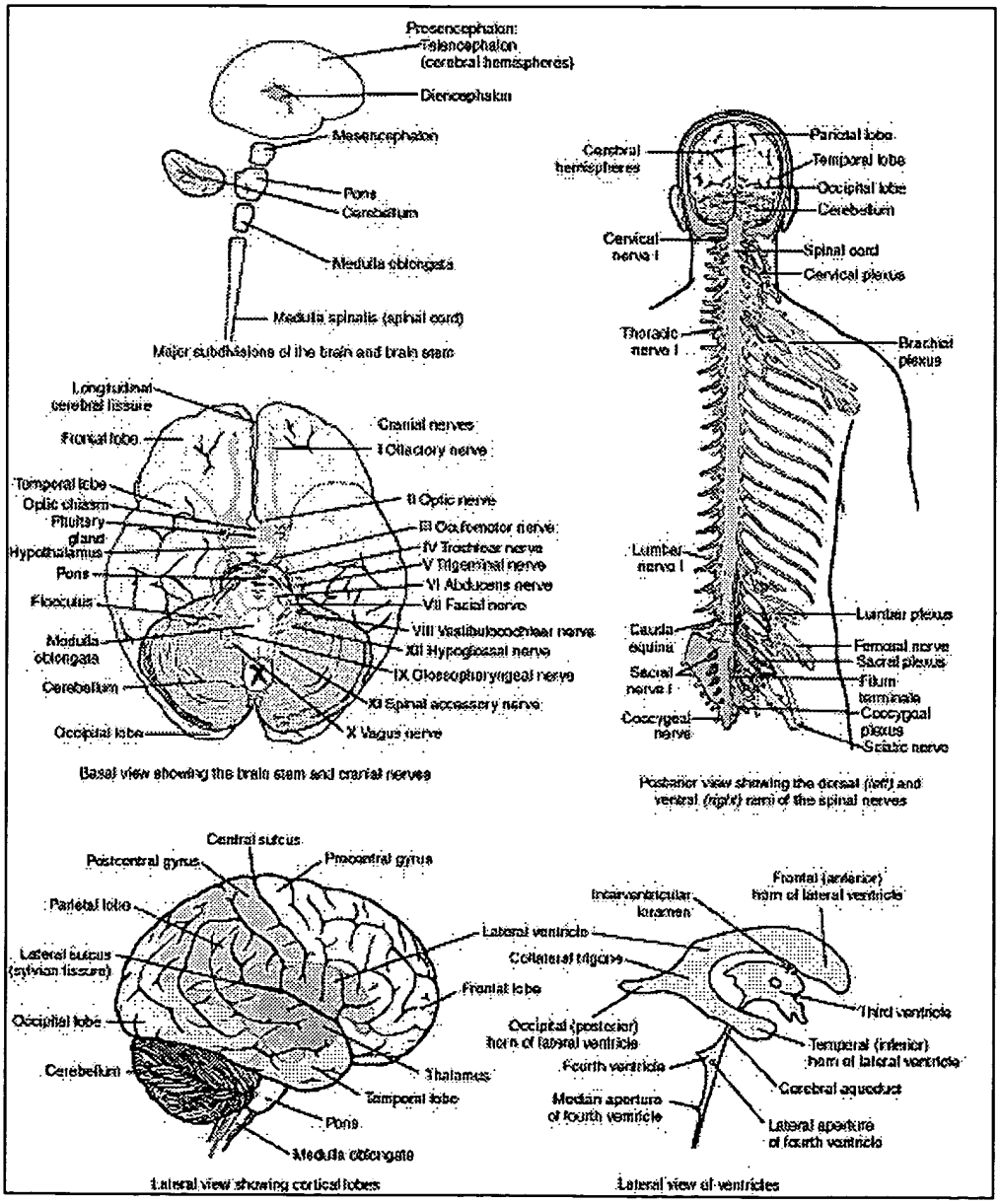

Plate 11—VARIOUS ASPECTS OF BRAIN AND SPINAL CORD

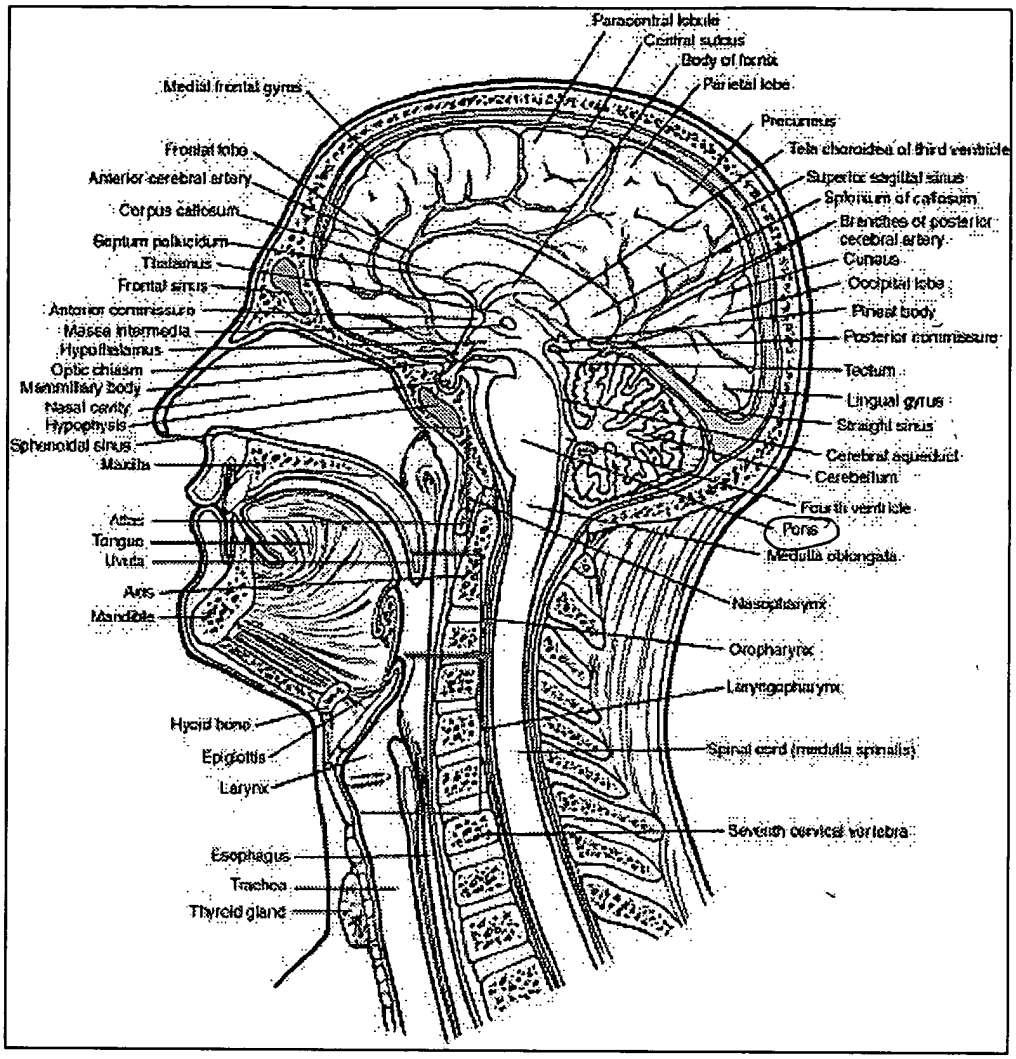

Plate 12—HEMISECTION OF THE HEAD AND NECK, SHOWING VARIOUS PARTS OF THE BRAIN[epIN RELATION TO OTHER STRUCTURES

olfactory brain, rhinencephalon, def. 1.

respirator brain, the congested, swollen brain of a patient who has been on a respirator longer than one day after suffering cerebral anoxia and ischemia; necrotic and autolytic changes begin to occur and the patient is comatose or brain dead.

split brain, a brain in which connections between the hemispheres, mainly the corpus callosum, have been severed or otherwise disrupted; done surgically on experimental laboratory animals and in humans to provide access to the third ventricle or to control epilepsy. See also *split-brain syndrome*, under *syndrome*, and *corpuscallosotomy*.

smell brain, rhinencephalon, def. 1.

wet brain, cerebral edema.

brainstem (brainstem) (br[amacr]n'stem") the stalklike portion of the brain connecting the cerebral hemispheres with the spinal cord and comprising the mesencephalon, pons, and medulla oblongata; the diencephalon is considered part of the brain stem by some. Called also *truncus encephalicus* [TA]. Also written *brain stem*.

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L7: Entry 75 of 75 File: USPT Oct 4, 1994

US-PAT-NO: 5352447
DOCUMENT-IDENTIFIER: US 5352447 A

TITLE: Immunotoxins for treatment of intracranial lesions and as adjunct to chemotherapy

DATE-ISSUED: October 4, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Johnson; Virginia	College Park	MD		
Youle; Richard J.	Garrett Park	MD		

US-CL-CURRENT: 424/183.1; 424/832, 514/12, 514/21, 514/8, 530/391.7, 530/394

CLAIMS:

We claim:

1. A method of treating central nervous system tumors or prophylaxing against metastatic lesions to the central nervous system comprising administering a tumor-inhibiting amount of a conjugate comprising a diphtheria toxin, wherein said diphtheria toxin lacks an active cell binding activity, attached to a moiety which binds to transferrin receptors, wherein said moiety which binds to transferrin receptors is selected from the group consisting of an anti-transferrin receptor antibody and transferrin, and wherein the mode of administration is intracranial or intrathecal.

2. A method of treating central nervous system tumors according to claim 1, wherein said mutant diphtheria toxin is selected from the group consisting of CRM102, CRM103 and CRM107.

3. A method of treating central nervous system tumors according to claim 2, wherein said mutant diphtheria toxin is CRM103.

4. A method of treating central nervous system tumors according to claim 2, wherein said mutant diphtheria toxin is CRM107.

5. The method of claim 1, wherein the conjugate is administered intrathecally.

6. The method of claim 1, wherein the conjugate is administered intraventricularly.

7. The method of claim 1, wherein the conjugate is administered into the cavity cavity left by a surgical resection of the tumor.

8. The method of claim 1, wherein the central nervous system tumor treated or

the metastatic lesion to the central nervous system prophylaxed against are secondary tumors arising from a primary breast malignancy.

9. The method of claim 1, wherein the central nervous system tumor treated or the metastatic lesion to the central nervous system prophylaxed against are secondary tumors arising from a primary lung malignancy.

10. The method of claim 1, wherein the central nervous system tumor treated or the metastatic lesion to the central nervous system prophylaxed against are secondary tumors arising from a primary prostate malignancy.

DOCUMENT-IDENTIFIER: US 6827931 B1
TITLE: Method for treating endocrine disorders

CLAIMS:

1. A method for treating an endocrine condition, the method comprising the step of intracranial administration of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G to the hypothalamus or pituitary of a patient, thereby treating a symptom of an endocrine condition by reducing a secretion of a hypothalamic or pituitary hormone or releasing hormone, wherein the endocrine condition is selected form the group consisting of gametogenesis, menstruation, acromegaly, gigantism, Cushing's disease, hypergonadism and hyperthyroidism.

2. The method of claim 1, wherein the botulinum toxin is botulinum toxin type A.

3. The method of claim 1, wherein the botulinum toxin is administered in an amount of between 10.sup.-2 units and 500 units.

5. The method of claim 1, wherein the botulinum toxin is administered to the median eminence region of the hypothalamus.

6. The method of claim 1, wherein the botulinum toxin is administered to the anterior pituitary.

7. The method of claim 1 wherein the botulinum toxin is administered to the posterior pituitary.

8. The method of claim 1, wherein the intracranial administration step comprises the step of implantation of a controlled release botulinum toxin system.

9. A method for treating an endocrine condition, the method comprising the step of intracranial administration of a therapeutically effective amount of a botulinum toxin type A to the hypothalamus or pituitary of a patient, thereby alleviating a symptom of an endocrine condition by reducing a secretion of a hypothalamic or pituitary hormone or releasing hormone, wherein the endocrine condition is selected form the group consisting of gametogenesis, menstruation, acromegaly, gigantism, Cushing's disease, hypergonadism and hyperthyroidism.

10. A method for treating an endocrine condition, the method comprising the steps of: (a) selecting a neurotoxin with hypothalamic releasing hormone suppressant activity: (b) choosing a hypothalamic target tissue which influences an endocrine disorder; and (c) intracranially administering to the target tissue a therapeutically effective amount of the neurotoxin selected, thereby treating the endocrine condition by reducing a secretion of a hypothalamic releasing hormone, wherein the neurotoxin is a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G and wherein the endocrine condition is selected form the group consisting of gametogenesis, menstruation, acromegaly, gigantism, Cushing's disease, hypergonadism and hyperthyroidism.

11. A method for treating hypergonadism, the method comprising the step of in vivo local administration of a therapeutically effective amount of a botulinum toxin type A to a cholinergically influenced hypothalamic tissue to a human patient, thereby alleviating a symptom of hypergonadism in the patient by reducing a secretion of hypothalamic hormone or releasing hormone.

12. A contraceptive method comprising the step of intracranial administration to a hypothalamus or

pituitary of a patient of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G, thereby reducing a hypothalamic or pituitary secretion of a hormone or releasing hormone required for gametogenesis.

13. The method of claim 12, wherein the botulinum toxin is botulinum toxin type A.

14. A method for inhibiting ovulation, the method comprising the step of intracranial administration to a hypothalamus or pituitary of a patient of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G, thereby reducing a hypothalamic or pituitary secretion of a hormone or releasing hormone which influences ovulation.

15. The method of claim 14, wherein the botulinum toxin is botulinum toxin type A.

16. A method for inhibiting sperm production, the method comprising the step of intracranial administration to a hypothalamus or pituitary of a patient of a therapeutically effective amount of a botulinum toxin selected from the group consisting of botulinum toxin types A, B, C.sub.1, D, E, and G, thereby reducing a hypothalamic or pituitary secretion of a hormone or releasing which influences sperm production.

17. The method of claim 16, wherein the botulinum toxin is botulinum toxin type A.

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L7: Entry 57 of 75 File: USPT Nov 11, 2003

DOCUMENT-IDENTIFIER: US 6645500 B1
TITLE: Method for down-regulating osteoprotegerin ligand activity

CLAIMS:

8. The method according to claim 7, wherein the epitope is selected from a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a P. falciparum CS epitope.

13. The method according to claim 8, wherein the Tetanus toxoid epitope is P2 or P30.

16. The method according to claim 1, wherein an effective amount of the OPGL polypeptide or the OPGL analogue is administered to the animal via a route selected from the group consisting of the parenteral route; the peritoneal route; the oral route; the buccal route; the sublinqual route; the epidural route; the spinal route; the anal route; and the intracranial route.

Summary of Invention Paragraph:
[0010] Although the cause of schizophrenia is not precisely known, there are several hypotheses regarding the causes. One hypothesis is that schizophrenia is associated with increased dopamine activity within the cortical and limbic areas of the brain. This hypothesis is supported by the therapeutic effects achieved by antipsychotic drugs that block certain dopamine receptors. In addition, amphetamine use may be associated with schizophrenia-like psychotic symptoms; amphetamines act on dopamine receptors.

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DOCUMENT-IDENTIFIER: US 6623742 B2
TITLE: Methods for treating fibromyalgia

CLAIMS:

1. A method for treating fibromyalgia, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a peripheral location of a body of a patient afflicted with fibromyalgia, wherein the peripheral location is not a locus of pain, and wherein the locus of pain and the site of administration are located within a same dermatome, thereby relieving a fibromyalgia pain for at least one month.

4. The method of claim 1 wherein the peripheral location is in a cranial area or a facial area of the patient, and wherein the locus of pain is at a fibromyalgia tender point.

5. The method of claim 1 wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F, and G.

6. The method of claim 1 wherein the botulinum toxin is a botulinum toxin type A.

8. The method of claim 1 wherein the botulinum toxin is administered with a needle.

9. The method of claim 1 wherein the botulinum toxin is administered by needleless injection.

10. A method for treating fibromyalgia pain, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a peripheral location of a body of a patient, wherein the patient has a locus of pain at a fibromyalgia tender point, and wherein the peripheral location is not at the locus of pain, and the locus of pain and the site of administration are located within a same dermatome, thereby relieving the pain for at least one month.

12. The method of claim 10 wherein the botulinum toxin is selected from the group consisting of botulinum neurotoxin types A, B, C, D, E, F, and G.

13. The method of claim 10 wherein the botulinum toxin is a botulinum toxin type A.

15. The method of claim 10 wherein the botulinum toxin is administered with a needle.

16. The method of claim 10 wherein the botulinum toxin is administered by needleless needleless injection.

17. A method for treating fibromyalgia, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a dermatome of a patient afflicted with fibromyalgia, wherein the dermatome encompasses 50% or more of a locus of pain, wherein the

administration is not at the locus of pain, thereby relieving a fibromyalgia pain for at least one month.

18. The method of claim 17 wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F, and G.

19. The method of claim 17 wherein the botulinum toxin is a botulinum toxin type A.

21. The method of claim 17 wherein the botulinum toxin is administered with a needle.

22. The method of claim 17 wherein the botulinum toxin is administered by needleless needleless injection.

23. A method for treating fibromyalgia pain, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin to a dermatome of a patient, wherein the patient has a locus of of pain at a fibromyalgia tender point, wherein the dermatome encompasses 50% or more of the locus of pain, and wherein the administration is not at the locus of pain, thereby relieving the pain for at least one month.

26. The method of claim 23 wherein the botulinum toxin is selected from the group consisting of botulinum neurotoxin types A, B, C, D, E, F, and G.

27. The method of claim 23 wherein the botulinum toxin is a botulinum toxin type A.

29. The method of claim 23 wherein the botulinum toxin is administered with a needle.

30. The method of claim 23 wherein the botulinum toxin is administered by needleless needleless injection.

31. A method for treating fibromyalgia, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin type A to a dermatome of a patient afflicted with fibromyalgia, fibromyalgia, wherein the dermatome encompasses 50% or more of a locus of pain which is at a fibromyalgia tender point, and wherein the local administration is not at the locus of pain, thereby relieving a fibromyalgia pain for at least one month.

32. A method for treating fibromyalgia pain, the method comprising the step of administering subcutaneously or intramuscularly a therapeutically effective amount of a botulinum toxin type A to a dermatome of a patient, wherein the patient has a locus of pain which is at a fibromyalgia tender point, wherein the dermatome encompasses 50% or more of the locus of pain, and wherein the administration is not at the locus of pain, thereby relieving the pain for at least one month.

DOCUMENT-IDENTIFIER: US 6113915 A
TITLE: Methods for treating pain

CLAIMS:

1. A method for treating pain, the method comprising the step of intraspinal administration of an effective amount of a botulinum toxin to a mammal, thereby alleviating pain experienced by the mammal, wherein the botulinum toxin is not attached to a non-neurotoxin protein.

2. The method of claim 1, wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F and G.

3. The method of claim 2, wherein the botulinum toxin is botulinum toxin type A.

4. The method of claim 1, wherein the botulinum toxin is administered in an amount of between about 10.sup.-3 U/kg and about 60 U/kg.

5. The method of claim 4, wherein the botulinum toxin is administered in an amount of between about 10.sup.-2 U/kg and about 50 U/kg.

6. The method of claim 5, wherein the botulinum toxin is administered in an amount of between about 10.sup.-1 U/kg and about 40 U/kg.

7. The method of claim 6, wherein the botulinum toxin is administered in an amount of between about 1 U/kg and about 30 U/kg.

8. The method of claim 6, wherein the botulinum toxin is administered in an amount of between about 1 U/kg and about 20 U/kg.

12. The method of claim 1, wherein the botulinum toxin is administered intrathecally.

13. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a cranial region of the central nervous system.

14. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a cervical region of the central nervous system.

15. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a thoracic region of the central nervous system.

16. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a lumbar region of the central nervous system.

17. The method of claim 12, wherein the botulinum toxin is administered intrathecally to a sacral region of the central nervous system.

18. The method of claim 1, wherein the administration step includes the steps of:

(a) accessing an intraspinal subarachnoid space of the mammal, and;

(b) injecting the botulinum toxin into the subarachnoid space.

31. A method for the in vivo attenuation of a nociceptive activity of a human patient, the method comprising the step of intraspinal administration to a human patient a therapeutically effective amount of a botulinum toxin, thereby causing an in vivo attenuation of a nociceptive activity.

33. The method of claim 31, wherein the botulinum toxin is selected from the group consisting of botulinum toxins A, B, C, D, E, F and G.

34. The method of claim 33, wherein the botulinum toxin is botulinum toxin type A.

35. A method for treating pain, the method comprising the steps of:

(a) selecting a botulinum toxin with antinociceptive activity;

(b) choosing a portion of the intraspinal region of a patient which influences a nociceptive activity; and

(c) intraspinally administering an effective amount of the botulinum toxin selected.

36. A method for treating pain, the method comprising the step of administering a pharmaceutical preparation to an intraspinal region or to a dorsal root ganglion of a mammal, thereby alleviating pain experienced by the mammal, wherein the pharmaceutical preparation comprises an effective amount of botulinum toxin which is essentially free of any non-neurotoxin protein.

The following definitions apply herein:

"About" means approximately or nearly and in the context of a numerical value or range set forth herein means ±10% of the numerical value or range recited or claimed.

"Local administration" means direct administration of a pharmaceutical at or to the vicinity of a site on or within an animal body, at which site a biological effect of the pharmaceutical is desired. Local administration excludes systemic routes of administration, such as intravenous or oral administration.

"Neurotoxin" means a biologically active molecule with a specific affinity for a neuronal cell surface receptor. Neurotoxin includes Clostridial toxins both as pure toxin and as complexed with one to more non-toxin, toxin associated proteins

"Intracranial" means within the cranium or at or near the dorsal end of the spinal cord and includes the medulla, brain stem, pons, cerebellum and cerebrum.

Methods for treating neuropsychiatric disorders comprise the step of intracranially administering a neurotoxin to a patient. The neurotoxin is administered in a therapeutically effective amount to alleviate at least one symptom of the disorder. The neurotoxin alleviates the symptoms associated with the disorder by reducing secretions of neurotransmitter from the neurons exposed to the neurotoxin.

A suitable neurotoxin may be a neurotoxin made by a bacterium, for example, the neurotoxin may be made from a *Clostridium botulinum*, *Clostridium butyricum*, or *Clostridium beratti*. In certain embodiments of